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THE EFFECT OF VASODILATOR DRUGS ON THE CIRCULATION OF THE EXTREMITIES

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THE obliteration of control of the sympathetic nervous system over the tone of the smooth muscles of the vascular bed may be accomplished by many methods. The indications for relieving pathologic vasospasms, or normal vasomotor tone in certain pathologic conditions, vary with the disease state which is being attacked. The release of vasoconstriction in generalized vasospastic states, or in such functional vascular conditions as Raynaud's disease or posttraumatic vasospasm, may be quite different from the release of vasoconstriction in the presence of organic arterial disease or occlusion. The purpose of our study has been to determine and compare the difference in effects on circulation of selective denervation of an extremity with generalized vasodilatation throughout the body. Also, it has been desirable to determine and compare the effect of sympathetic nerve block on the circulation of a given area with the effect of vasodilator compounds in the various tissues of which the extremity is composed.

It is well known that the primary function of the circulation in the skin and superficial tissues is regulation of body temperature and nutrition in these tissues, whereas the circulation to the muscle of an extremity is supplying an organ of motion. Factors which control the blood flow through the 2 types of tissue are quite different. It is therefore desirable to find the method of vasodilatation which is most applicable to the condition being treated.

Several compounds designed to produce vasodilatation through blockading of the sympathetic nervous system at some point have been released by numerous pharmaceutical laboratories, and other compounds to be used in

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the treatment of peripheral vascular disorders are being investigated. Many reports have appeared in the literature concerning the efficacy of using these preparations. It is unquestioned that certain of the drugs are able to increase blood flow in selective areas of the body in normal individuals. The reports that have been made recently, however, have been based largely upon clinical trial and the patient's subjective evaluation of improvement, rather than upon objective measurements.

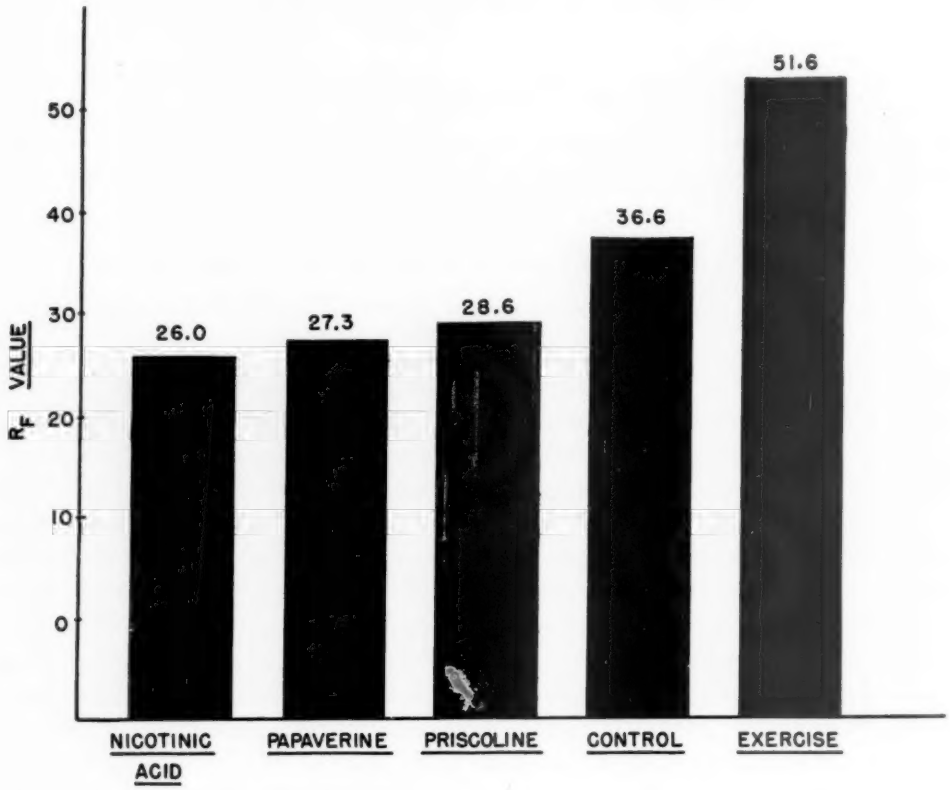

Fig. 1.—Rate of removal of sodium 24 expressed as per cent removed in 10 minutes in control group following the administration of drugs and after exercise.

In our laboratories several methods of study have been utilized. Previous reports[1-3] have described a method of securing an index to blood flow in muscle by injecting into the gastrocnemius muscle a small quantity of radioactive sodium 24 as a hypotonic solution and then measuring with a suitable electromechanical device the disappearance from the extremity of this crystalloid following its mobilization. This study is carried out in a constant temperature room at 78° F. and with the individual lying with the legs elevated at an angle of 30 degrees. The standard rate of disappearance of the radioactive sodium is determined over a period of 10 minutes.

In a series of 60 control extremities upon which this study was performed, it was found that, in the resting state, 36.6 per cent of the intramuscularly-injected sodium chloride would be removed in 10 minutes (Fig. 1). Upon exercise of the extremities by rhythmic contraction of the gastrocnemius and

soleus muscles, it was found that a very potent stimulus to the removal of sodium was created. Exercise in these individuals resulted in the increased rate of removal of 51.6 per cent in 10 minutes. Creation of hyperemia through the temporary production of muscle ischemia by the application of a tourniquet resulted in even greater rates of removal, but these persisted for only a short period of time.

Utilizing the same group of normal controls, the commonly used vasodilator compounds were studied. After the 10 minute interval in which the rate of removal of the radioactive sodium chloride was determined, one of the vasodilator preparations was injected intravenously. It was then determined how rapidly the sodium was removed following the administration of this

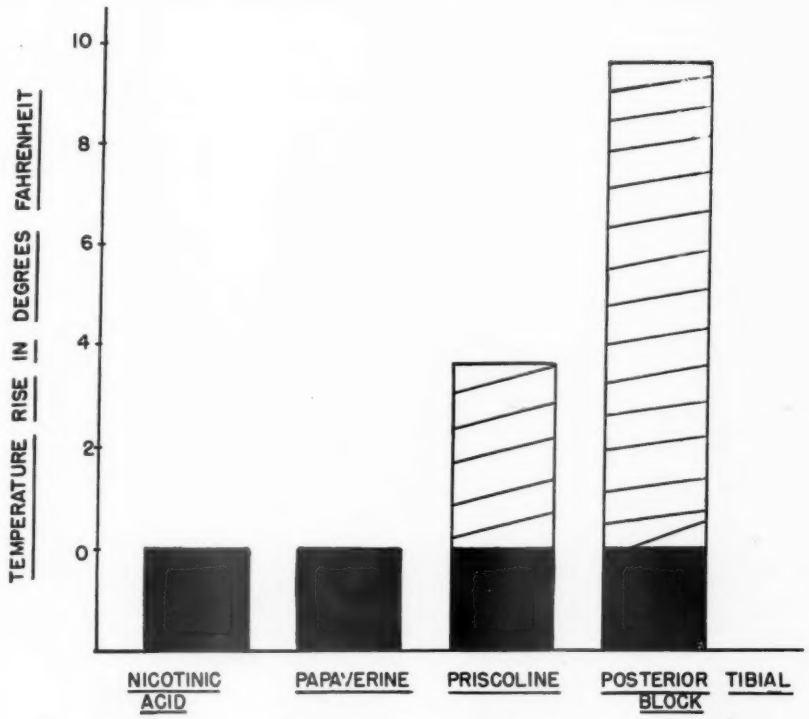

Fig. 2.—Change in skin surface temperature following the administration of drugs and posterior tibial nerve block.

vasodilator drug. It was found that the vasodilator drug uniformly diminished the rate of uptake of the radioactive sodium from the muscle. The results, shown in Fig. 1, were pronounced and consistent. In the patient who has been treated by lumbar sympathectomy, it was similarly found that the rate of removal of radioactive sodium chloride was markedly diminished, but also there were increases in skin surface temperatures.

Supplementing this study, blood flow determinations were made by measurement of skin surface temperatures and plethysmographic studies in which the vasodilator preparations of alcohol, nicotinic acid, papaverine, Priscoline, and C7337 were tested. The subjects here were again studied in a room at 78° F. under basal conditions. Of the vasodilator compounds tested, Priscoline and C7337 were the only agents which elevated skin surface temperatures

in the digits of normal extremities and which, as evidenced by plethysmographic responses, resulted in an increase in blood flow (Figs. 2 to 4).

Then, in an effort to simulate the pathologic state, vasospasm was induced in normal individuals by cooling the room to 68° F. After a period of 30 minutes, plethysmographic responses were studied and skin surface temperatures were determined. The individuals were then given either from 32 to 64 mg. of papavarine, 50 mg. of nicotinic acid, or 25 mg. of Priscoline. Observations were carried out thereafter for a period of 1 hour. Papaverine and nicotinic acid did not significantly change either skin surface temperatures in the digits or plethysmographic responses. Priscoline, however, effected an increase in these responses, but one which was not nearly so great as that accomplished by posterior tibial nerve block or sympathectomy.

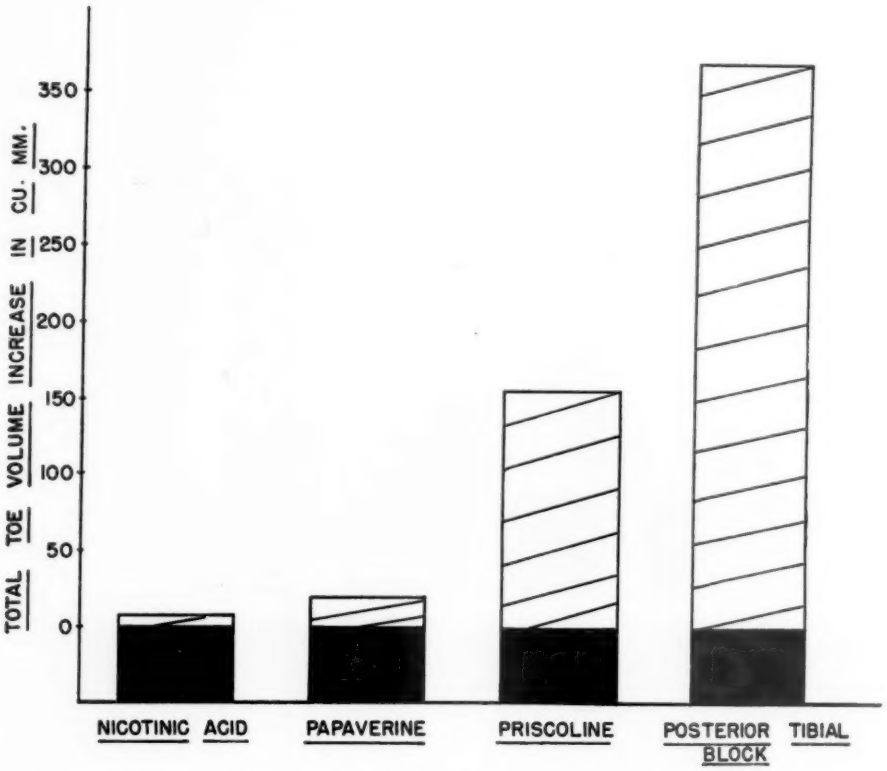

Fig. 3.—Change in toe volume following administration of drugs and posterior tibial nerve block.

In patients with organic obliteration of the arteries as a result of Buerger's disease, arteriosclerosis, or embolism, or with actual ligation, in which one extremity remained normal, the same methods of study were carried out. Responses from the normal, as well as the diseased, extremity were obtained for control study purposes. It was found that in this group of individuals, while blood flow increased in the normal extremity as reflected by increases in skin surface temperatures, volumes of the digits, and pulse volumes, that in the diseased extremity there was either no significant change or the blood flow was reduced.

CASE REPORTS

Buerger's Disease.—This 54-year-old white man first noticed the onset of intermittent claudication in the right leg at the age of 27. While receiving conservative therapy at the age of 38, he developed gangrene of the right foot, which eventually necessitated amputation of the lower leg. Symptoms in the left leg remained relatively mild, and there was no significant increase in the extent of the disease. At the age of 49, intermittent claudication was first noticed on the left, and there was gradual increase in his intolerance for activity. Two years later a bilateral lumbar sympathectomy was performed, and an ulceration on the left lower extremity subsequently healed.

The patient continued to smoke cigarettes heavily.

Three months prior to this study, the patient's symptoms in the left lower extremity became exaggerated. Ulceration developed on the dorsum of the left foot at the base of the great toe. Examination of the extremities at this time revealed trophic changes in the skin and its derivatives. There was only minimal pallor on elevation and slight rubor on dependency. Sweating was present over the left leg, except for a small area on the lateral aspect of the foot and of the lower third of the left leg. Dorsalis pedis pulsation was absent on the left, but good posterior tibial pulsation was present.

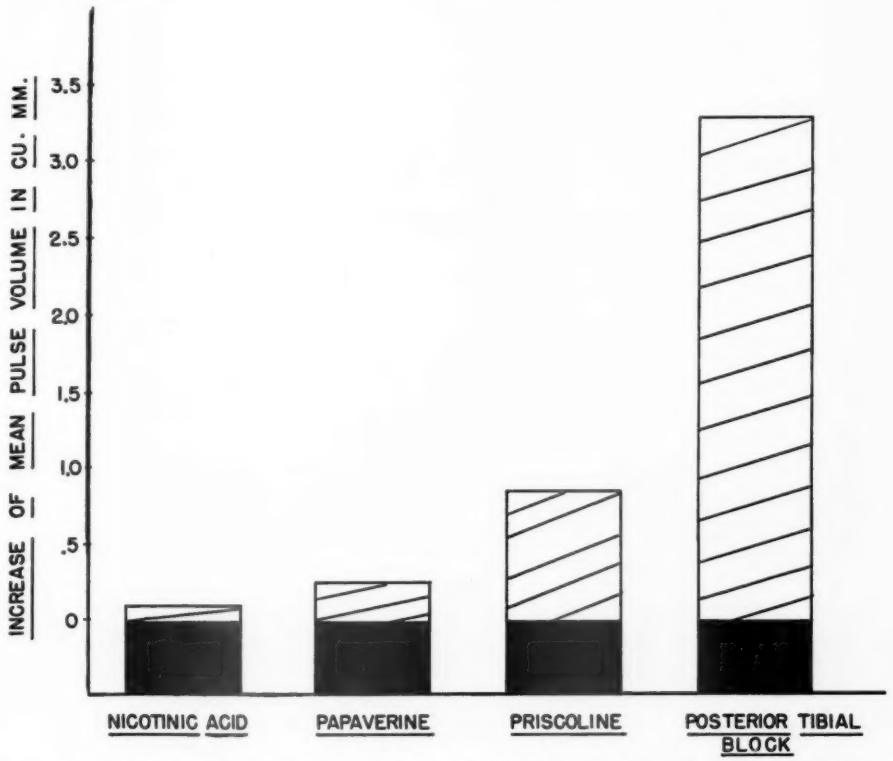

Fig. 4.—Increase in pulse volume following the administration of drugs and posterior tibial nerve block.

Oscillometric readings were normal on the left, but were diminished at the right popliteal region. The rate of removal of radioactive sodium from the gastrocnemius muscle was 45 per cent in 10 minutes.

Injection of 0.5 mg. per kilogram of C7337 resulted in an immediate decrease in pulse volumes (Fig. 5). The original pulse volume levels were attained gradually over a period of 15 minutes. Skin surface temperatures of the toes did not rise, but dropped 1 degree during the period of observation. The patient's pulse rate markedly increased, and the blood pressure transiently declined with the patient in the recumbent position. A marked postural hypotension was present at the end of 35 minutes.

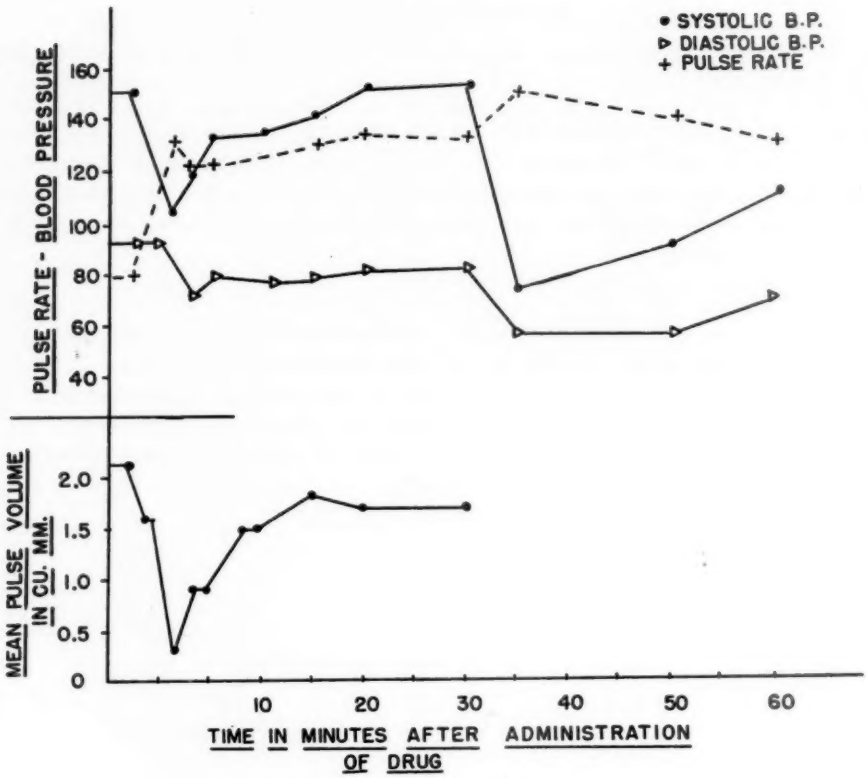

Fig. 5.—Buerger's disease.

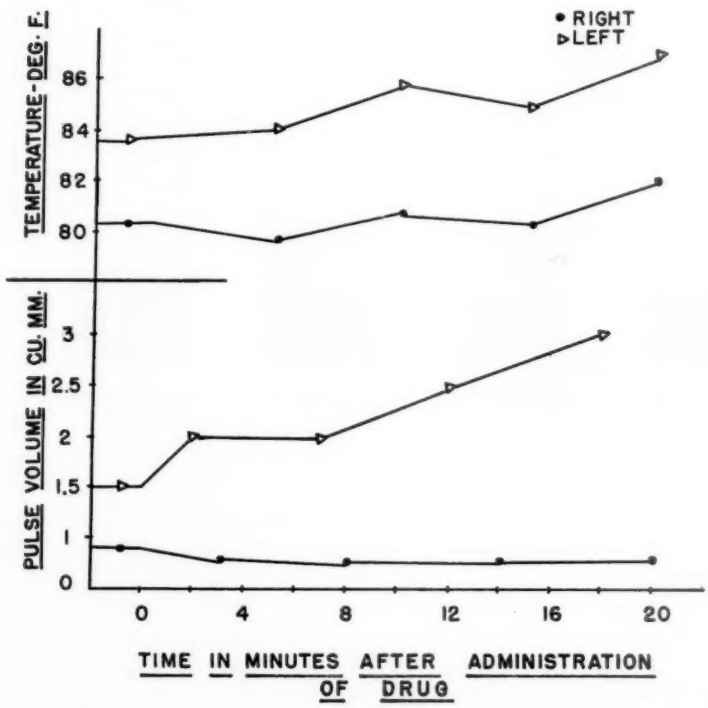

Fig. 6.—Thrombosis of the right superficial femoral artery.

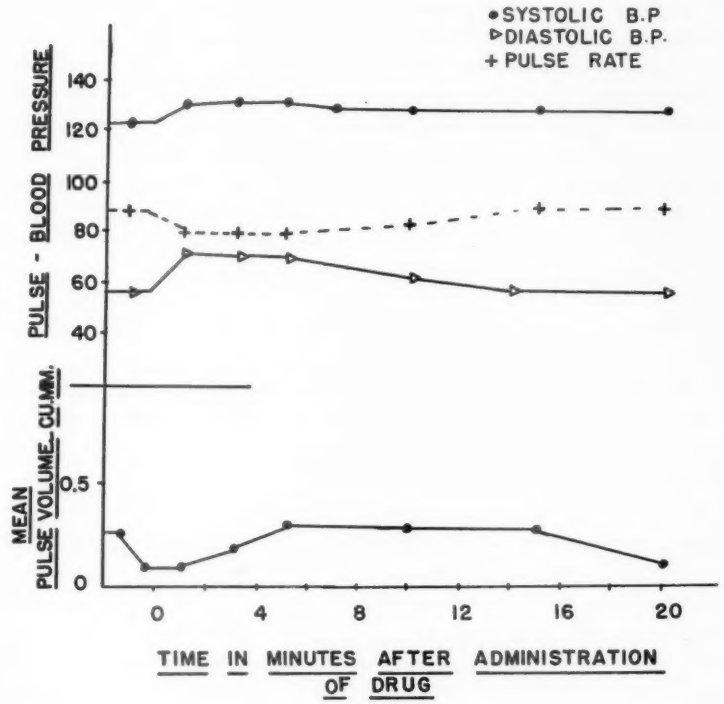

Fig. 7.—Ligation of the popliteal artery.

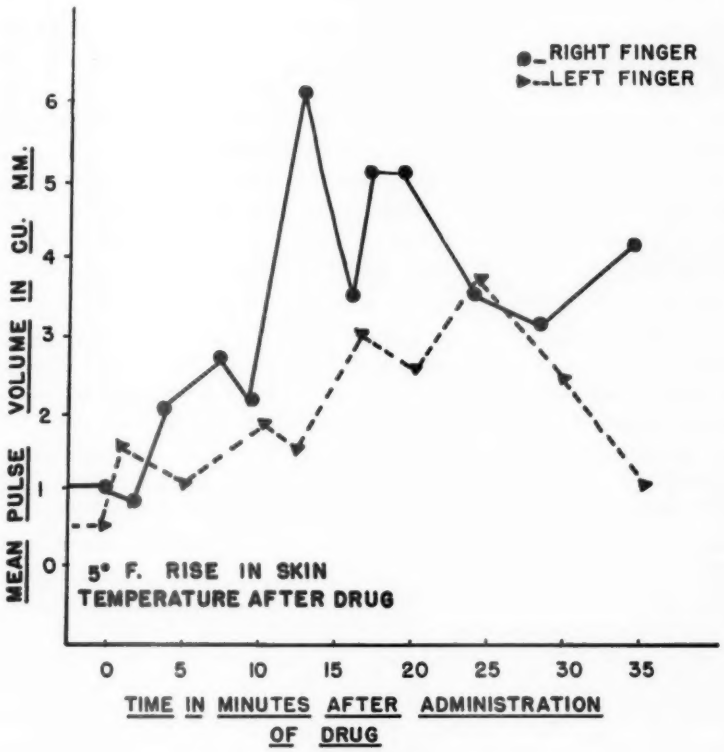

Fig. 8.—Raynaud's disease.

Thrombosis of the Right Superficial Femoral Artery.—This 61-year-old Jewish man had been a known mild diabetic for 5 years. Four months prior to this study, he noticed the sudden onset of pain in the right calf muscle while taking a shower. His activity had been limited by pulmonary tuberculosis, and he was, therefore, unable to evaluate the functional incapacity in the extremity. Examination revealed slight trophic changes in the skin on both lower extremities. The right lower extremity became pallid on elevation and ruborous on dependency. No arterial pulsations could be palpated below the femoral region on the right.

Instrumental examinations revealed markedly diminished oscillometric excursions at the right knee and ankle, and low skin surface temperatures bilaterally. The removal factor of intramuscularly injected radioactive sodium from the right calf muscle was 20 per cent in 10 minutes.

Following the intravenous administration of 25 mg. of Priscoline, there was a moderate increase in pulse volumes in the toes of the left extremity (Fig. 6). In the right extremity, however, pulse volumes decreased. In 20 minutes there was a 1½ degree rise in skin surface temperatures on the right and a 3 degree rise in skin surface temperatures on the left.

Ligation of the Popliteal Artery.—This 40-year-old white man had sustained a bullet wound of the popliteal space in the left leg 4 years previous to this examination. After that time, he noticed swelling of the extremity, increased prominence of the veins, coldness of the foot, and discoloration of the extremity on dependency. An ulceration measuring 5 cm. in diameter developed on the lateral aspect of the left leg 1 year prior to examination. The ulceration failed to respond to treatment and gradually enlarged.

Physical examination on admission revealed diffuse swelling of the left lower extremity. There were numerous areas of pigmentation and a large ulceration, 7½ cm. in diameter, on the lateral aspect of the leg. The left foot was ruborous in the horizontal position and demonstrated mild pallor on elevation. Arterial pulsations were everywhere present. A pulsating expansile mass could be felt in the popliteal region, and there was a continuous thrill and bruit, with systolic accentuation.

Instrumental examination revealed markedly increased oscillometric excursions at the popliteal level. Skin surface temperatures were normal. Intramuscularly injected radioactive sodium disappeared at the rate of 56 per cent in 10 minutes.

An operation was performed in which an arteriovenous communication between the popliteal vessels was excised, and the popliteal artery was ligated.

Nine days after operation studies were performed following the injection of C7337 in dosages of 0.5 mg. per kilogram (Fig. 7). There was a rise in pulse volumes which persisted for approximately 10 minutes, but then declined to lower than control levels. There were no increases in total toe volumes. Skin surface temperatures on the affected side decreased.

Raynaud's Disease.—A 46-year-old white nurse reported that for 6 years her fingers had blanched on cold exposure. The attacks became more frequent in severity, and could even be induced by emotion. She noticed gradual thickening of the skin of her fingers, a feeling of tightness, and slight limitation of motion. For 3 months prior to the initial examination she had developed small ulcerations on the tips of her affected fingers.

Examination revealed moderate scleroderma of the fingers of both hands. An ulceration with a necrotic base was present on the tip of the right index finger. Arterial pulsations were normal. Skin surface temperatures were normal, as were oscillometric excursions. Complete blanching of the fingers could be produced by emersion of the hands in ice water or other exposure to cold.

Following exposure in a room at 78° F., the patient was given 25 mg. of Priscoline intravenously. Pulse volumes in the digits of both hands immediately increased, and there was a 5 degree rise in skin surface temperatures of the digits (Fig. 8). During the period of observation, there was no return of the digital blanching. In this case, Priscoline was effective in the release of vasospasm in the extremities, producing objective evidence of increased blood flow to the parts.

Hyperactive Vasomotor State.—This 41-year-old housewife had noticed excessive coldness and perspiration of the hands and feet for many years. For the 1½ years prior to this

examination she had noticed some duskiness of the middle fingers of both hands on exposure to cold. This discoloration was associated with feelings of numbness, tingling, stiffness, and swelling.

Physical examination of the upper extremities revealed them to be essentially normal in appearance. Arterial pulsations were normal at all levels. There were no abnormal color changes on positional maneuver. There was no evidence of a cervical rib or of a scalenus anticus syndrome.

Instrumental examination revealed normal oscillometric excursions. Measurement of skin surface temperatures showed below-normal levels.

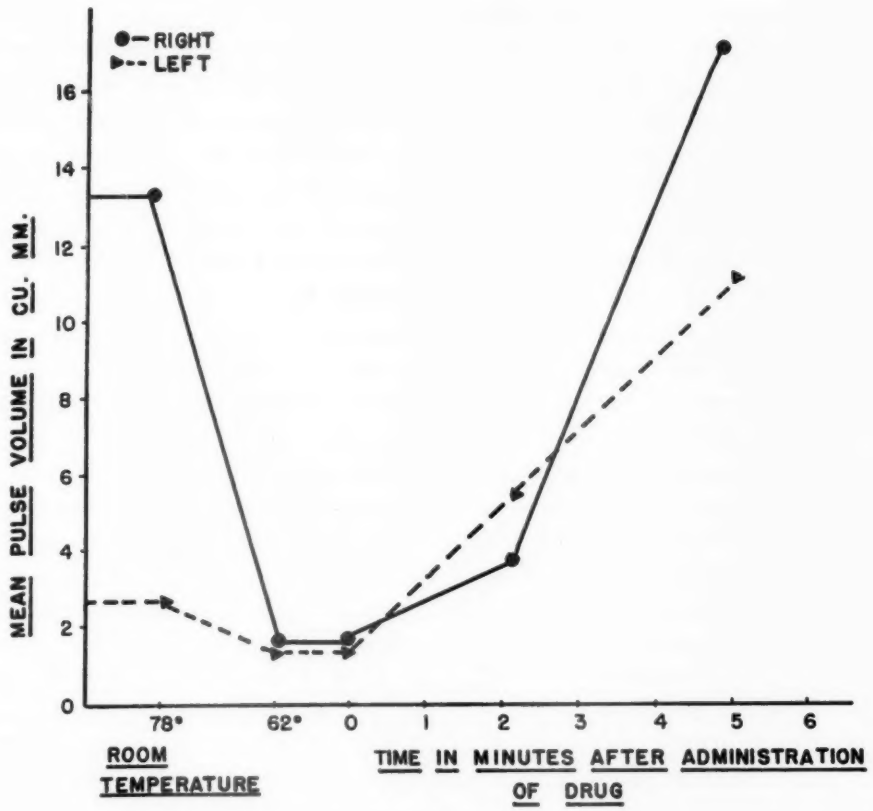

Fig. 9.—Hyperactive vasomotor state.

Exposure in a room at 62° F. resulted in a marked decrease in the average pulse volumes of the index fingers of both hands (Fig. 9). Twenty-five milligrams of Priscoline were then given intravenously, with an immediate rise in pulse volumes, as outlined in the chart, and a concomitant 5 degree rise in skin surface temperatures of the digits. In this condition there was increased blood flow to the digits, as reflected by skin surface temperatures and increased pulse volumes immediately following the administration of Priscoline.

DISCUSSION

The heart serves as a pump, supplying a given quantity of blood per minute into the hydraulic system of the body. The flow of blood in the system is dependent upon the alternate opening and closing of the vascular tree, much like a canal system with its locks supplying water to the area directed by the over-all control mechanism. As long as the output of the heart, or pump, remains constant, the flow of blood is dependent upon the patency of the chan-

nels, and the number of channels, or locks, open. It would, therefore, seem obvious, as postulated in the theory of hemometakinesia by DeBakey, Burch, and associates,[4] that augmentation of the circulation to one portion of the body at a given time must occur at the expense of that to another portion. Also, during a state of health, there will be a constant fluctuation in the flow of blood through the various viscera of the body as the needs of the various parts change.

A similar circulatory process operates within the tissues of a single extremity. Thus, with increase in demand for blood in the skeletal muscles during activity, there may be peripheral vasoconstriction with diminution in flow through the skin and superficial channels. Similarly, in a period of rest, when temperature regulaton may be the predominating need, the blood flow through the skin should be greatly increased over that in the muscle. In conditions of exaggerated vasodilatation in the extremities as a result of sympathetic denervation, arteriovenous shunts are opened, as observed by Harpuder and others,[5] with great increase in the superficial blood flow in the extremities, but at the expense of the blood flow to other areas.

Without increased cardiac output, an increase in blood flow to one part is always affected by balancing or deprivation of blood flow to another. Since the flow of blood in the body obeys the hydraulic principles of an elastic circuit, the flow will always be through channels of least resistance. It is obvious, therefore, that selective vasodilatation in a given area will result in an increase in blood flow to that area. Generalized vasodilatation will result in a more equal distribution of blood flow through paths of equal resistance, but will not increase blood flow in a given area. In the presence of organic arterial disease it would be expected that the diseased extremity would offer more resistance to dilatation than the undiseased or uninjured portion of the body, and hence, producing a state of generalized vasodilatation, would be a relatively ineffective method of increasing blood flow in the diseased extremity. In the instance of a ligated or thrombosed femoral artery, greater resistance would be encountered to increasing blood flow to the foot in that extremity through the small collateral channels than in a normal opposite extremity. If, however, the prevention of vasoconstriction in 2 areas similarly affected by a functional disorder is desired, the equal and bilateral inhibition of vasomotor tone should be effective.

The role of the sympathetic nervous system in controlling blood flow and its relative importance in this role varies with the tissues concerned. Ischemia, as a result of anoxemia or exercise, is a much more potent stimulus to the circulation of blood in the muscle than is autonomic activity, whereas circulation of blood in the skin and superficial channels, as it has an important function as a regulator of body temperature, is directly influenced by the autonomic nervous system. It is, therefore, obvious that generalizations should not be made as to the efficacy of the various drugs and sympathetic blockading agents, as well as sympathectomy, in increasing blood flow to the extremities in normal individuals, in individuals with vasospastic phenomena, and in individuals with organic arterial occlusion.

The therapeutic implications are obvious. The patient with arterial insufficiency of an organic nature in an extremity is concerned primarily with keeping the envelope of the body intact. Inability to walk, while incapacitating, is a matter only of displeasure; however, ulcerations in the skin, gangrene, or neuritic disturbances result in severe pain and inability to lead any type of comfortable existence. In the treatment of these individuals the first concern is to maintain viability of the skin, and, secondarily, to increase blood flow in the muscles. Since autonomic activity in the extremity can be influenced, the method of selective denervation has gained wide popularity. With selective denervation of the extremity, a great deal is accomplished if trophic changes can be prevented or arrested and the healing of wounds or ulcerations can be effected. Benefit to the muscle is also a frequently observed phenomenon. It is obvious that in organic arterial diseases, localized vasodilatation only should be employed. As has been shown previously, generalized vasodilatation may be not only ineffective, but definitely harmful.

It is hoped that, in the future, selective denervation can be achieved by chemical means by direct intra-arterial injection of some of the vasodilator compounds. If, through intra-arterial administration of these compounds, the effect can be limited to a desired area and to a lesser degree to other areas, the same therapeutic effects would be achieved as those brought about through sympathectomy.

In the treatment of primarily vasospastic conditions, such as posttraumatic vasospastic states or Raynaud's disease, the problem is one of quite a different nature. With the actual caliber of the peripheral vessels remaining unobstructed, there is need only to decrease the sensitivity of the peripheral vessels to vasomotor control. The administration of vasodilator compounds prior to the reception of the vasomotor stimuli has brought results of marked clinical improvement. This same improvement has been noted as a result of decreased sympathetic outflow as produced by sedation with barbiturates, introduction to a warm climate, emotional rehabilitation through personal readjustments or hormone administration, or other similar therapy. In certain vasospastic conditions it is believed that these compounds may have a valuable function, but only in such conditions should these be used.

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EXPERIENCES WITH LIGATION AND HEPARIN IN THROMBOEMBOLIC DISEASE

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DURING the 5 year period from Jan. 1, 1945, to Dec. 31, 1949, the members of the Surgical Department of the Hospital of the University of Pennsylvania were greatly interested in thromboembolic complications and utilized several methods of therapy to reduce their incidence. The results in 27,802 patients operated upon during this period on the general surgical, urologic, and neurosurgical services have been carefully recorded and have now been analyzed. Recognizing that studies of specific prophylactic and therapeutic measures were in progress elsewhere, reliance was not placed on any one of the currently recommended methods of prophylaxis and treatment. Rather, an effort was made to stress the use of several supposedly helpful general prophylactic measures and to individualize the use of anticoagulants and proximal vein ligation once the diagnosis of thrombosis was made. The general plan of management, which has been adhered to in so far as possible, is shown in Table I.

PHLEBOTHROMBOSIS AND THROMBOPHLEBITIS

Of the 27,802 patients operated upon, a diagnosis of phlebothrombosis or thrombophlebitis was made during the postoperative period in 181, an incidence of 0.651 per cent (one in 153 operations). Superficial phlebitis of the arm veins and of the superficial saphenous system are not included. Although patients with minimal signs and symptoms were considered to have phlebothrombosis, and those with massive edema, a sharp temperature elevation, and vasospasm were diagnosed as having acute thrombophlebitis, many patients were in a borderline category in which it was not certain which of the 2 conditions predominated. Thirty-four, or 18.8 per cent, of the patients were below the age of 40. Nineteen were treated "conservatively," that is, without ligation or anticoagulants. Six of these had procaine blocks of the lumbar sympathetic ganglia. The other 162 patients were treated by ligation, with anticoagulants, or both, as follows: superficial femoral vein ligation, 69; superficial femoral vein ligation and heparin, 21; iliac vein ligation, 3; vena cava ligation, 3; heparin, 48; Dicumarol, 11; and heparin and Dicumarol, 7. Patients who had nonfatal pulmonary infarction or fatal pulmonary embolism after a diagnosis of phlebothrombosis or thrombophlebitis had been made are discussed below. An additional 21 patients who were not operated upon, or were on other services, and in whom a diagnosis of phlebothrombosis or thrombophlebitis was made, had superficial femoral vein ligation.

NONFATAL PULMONARY INFARCTION

In 57 patients (21.2 per cent of the patients diagnosed as having postoperative thromboembolic disease) the diagnosis of nonfatal pulmonary infarction was made on the basis of chest pain, cough, hemoptysis, x-ray examination, electro-

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TABLE I. MANAGEMENT OF THROMBOEMBOLIC DISEASE; MEASURES USED AGAINST THROMBOEMBOLIC DISEASE FROM 1945 TO 1949, INCLUSIVE

A. Prophylaxis	
Routine measures: "promenade in bed"; frequent change of position in bed; early ambulation; compression bandages, applied before anesthesia and operation and maintained until discharge; deep breathing exercises; prompt replacement of blood loss; avoidance of abdominal distention and of heavy sedation; prevention of dehydration, electrolyte imbalance, and hypotension.	
In patients in whom there is an unusual risk of a thromboembolic complication, especially when there is a history of previous embolism, prophylactic use of anticoagulants and prophylactic superficial femoral vein ligation (patients to be selected by the chief of service).	
B. Treatment	
Phlebothrombosis	Bilateral superficial femoral vein ligation or anticoagulants, at the discretion of the chief of service
Acute thrombophlebitis	Lumbar sympathetic block or anticoagulants
Extension of thrombus proximal to femoral vein	Anticoagulants
Suppurative iliofemoral or pelvic thrombophlebitis.	Ligation of the iliac veins or vena cava
Pulmonary infarction without dyspnea.	Bilateral superficial femoral vein ligation or anticoagulants at the discretion of the chief of service
Massive pulmonary embolism	Heparin 50 mg. intravenously at once; in addition, atropine, papaverine, oxygen, and morphine

cardiographic tracings, and the clinical course. This represents an incidence of 0.205 per cent (one in 487 operations). In most instances pleuritic pain was the principal symptom and the clinical course was not significantly altered by the infarction. In 7 patients there were dyspnea, cyanosis, and prostration. Twenty-six patients were moderately or completely ambulatory before infarction occurred; 14 were up in wheel chairs or had just begun ambulation; the remaining 17 had not been out of bed. In 33 patients there was no apparent evidence of thrombosis prior to infarction. In 11 there were fever and tachycardia which were thought to be due to some other condition already diagnosed, while in the remaining 13 there was evidence of thrombosis of the leg veins. It is significant that 5 of these patients had protective therapy prior to infarction. Three had superficial femoral vein ligations and, after infarction occurred, were heparinized. The fourth had an infarct after a unilateral superficial femoral vein ligation was performed, and the contralateral superficial femoral was then ligated. The fifth was heparinized when leg signs and symptoms appeared and, when infarction occurred, was ligated. Seven of the 57 patients with nonfatal infarction were given no treatment other than bed rest. They had but the single embolism. The remaining 50 were treated as follows: superficial femoral vein ligation, 15; superficial femoral vein ligation and heparin, 10; vena cava ligation, 1; iliac vein ligation, 1; heparin, 15; heparin and Dicumarol, 6; and Dicumarol, 2. Two patients had additional infarcts following ligation and heparin therapy. In 2 other patients a septic temperature curve and shadows in the lower lung field on x-ray examination persisted for nearly 3 weeks but resolution finally occurred without demonstrable abscess formation.

FATAL PULMONARY EMBOLISM

Fatal pulmonary embolism occurred in 31 (11.5 per cent of the patients with thromboembolic disease), an incidence of 0.11 per cent (1 in 896 operations) of all the operative patients. Eight other patients died with symptoms and signs which were strongly suggestive of massive pulmonary embolism but, since autopsies were not performed, they are not included in this analysis. It is our opinion that a pulmonary embolus was the cause of death in at least one-half of them.

Age and Sex.—Only 4 of the 31 fatal embolisms occurred in patients under 40 years of age. Two were neurosurgical patients who had been in coma for a prolonged period of time. One, 35, had a malignant brain tumor and the other, 23, had tuberculous meningitis. The third was a 14-year-old boy who had had a Blalock operation done for the tetralogy of Fallot. A superficial femoral vein graft was used to bridge a defect between the left subclavian and pulmonary arteries and death occurred suddenly on the fifth postoperative day. At autopsy a large embolus was found occluding the stenotic infundibulum and pulmonic valve. It was not determined whether the embolus originated at the site from which the vein graft was taken. The fourth patient was a 38-year-old man who had an uneventful gastric resection for duodenal ulcer. On the ninth postoperative day slight soreness and tenderness of the left calf were noted. Intramuscular heparin therapy was started and after five days the signs and symptoms had subsided. He was discharged, and 24 hours later, when apparently well, he died suddenly. At autopsy a large embolus was found occluding the main pulmonary artery.

All other patients were 48 years of age or older (Table II).

Sixteen of the fatal embolisms occurred in males and 15 in females.

Disease and Site of Operation.—The surgical diseases which the patients had and the operative procedures performed are shown in Table II. Nearly

TABLE II. FATAL PULMONARY EMBOLISM, 1945 TO 1949, INCLUSIVE

DIAGNOSIS	NUMBER OF PATIENTS	AGE	OPERATION
Chronic cholelithiasis	1	60	Cholecystectomy
Appendical abscess	3	67, 73, 53	Appendectomy and drainage
Carcinoma of breast	2	72, 68	Radical mastectomy
Benign prostatic hypertrophy	2	76, 75	Transurethral resection
Strangulated inguinal hernia	1	68	Resection
Malignant brain tumor	5	48, 35, 58, 48, 58	Partial removal
Carcinoma of the lung	2	52, 70	Pneumonectomy
Carcinomatosis	2	68, 54	Biopsy
Carcinoma of the prostate	2	72, 68	Transurethral resection
Hip fracture	2	85, 76	Pinning
Multiple lung abscess	2	55, 57	Pneumonectomy
Tic douloureux	1	50	Fifth nerve section
Tetralogy of Fallot	1	14	Blalock operation
Incisional hernia	1	63	Repair
Strangulated femoral hernia	1	70	Resection
Tuberculous meningitis	1	23	Ventriculogram
Pyloric obstruction	2	50, 38	Gastric resection
Total	31		

one-half had malignant tumors. The majority of the remainder were seriously ill because of their primary disease or postoperative complications, or because they were old and debilitated.

Ambulation.—Since reliance was placed on early and continued exercise in bed and on early ambulation as prophylactic measures, the actual amount of activity of the patients in the fatal embolism group was carefully studied. Nineteen of the patients had not been out of bed following operation. The majority of these were too ill to do active and continued bed exercises, or often even to move themselves in bed. Six patients were hypoactive, both in and out of bed. The remaining 6 satisfied all of our exercise criteria and had been actively ambulating.

Site of Origin of the Embolus.—In 7 patients the site of origin of the embolus which caused death was not determined at post-mortem examination. In 6 of these the legs were not examined, while in the seventh no evidence of thrombosis could be found in the veins of the lower extremities or elsewhere in the venous system. In the remaining 24 patients the sites of origin appeared to be clear cut to the pathologists and were as follows: femoral veins, 10; iliac veins, 7; internal hypogastric veins, 2; popliteal veins, 2; calf veins, 1; vena cava, 1; and right auricle, 1. In only 3 was the apparent source a vein smaller than the femoral. The patient in whom the right auricle was thought to be the source of the embolus did not have an examination of the leg veins, which cannot, therefore, be excluded.

Warning.—The clinical records were studied to determine whether any warning signs or symptoms existed prior to fatal embolism. All staff members and residents were "thromboembolism conscious" and examined the legs, particularly of sick and elderly patients, at frequent intervals. Unexplained elevation of rising temperatures and pulse rates was considered with particular suspicion. In 16 patients there was no apparent clinical evidence that major thrombosis had occurred. In an additional 7 patients an elevated or rising pulse and temperature were considered to be due to the primary disease or to a complication already diagnosed. In 23 patients, or 74 per cent, the first striking clinical evidence of a thromboembolic complication was massive pulmonary embolism. In the remaining 8 patients there was definite evidence of thrombosis of the leg veins before embolism occurred. Two of these were treated with heparin. One was the 38-year-old man, previously described, who had a massive embolism 24 hours after heparinization was stopped. The other was a 48-year-old comatose neurosurgical patient with a malignant brain tumor which had been partially removed. On the eleventh postoperative day swelling of the left leg was noted and heparinization was begun. After 4 days of intramuscular heparin therapy, 0.075 Gm. every 6 hours, she suddenly died of a massive pulmonary embolism. The clotting time had been maintained between 20 and 45 minutes and, 3½ hours before death, was 38 minutes. The site of origin was found at autopsy to be the left iliac vein and there was evidence of previous small pulmonary infarcts, not diagnosed clinically.

Prophylaxis.—Specific prophylactic measures, other than those listed under "General" in Table I, were employed in only 2 patients. Bilateral superficial femoral vein ligation was performed in both patients. Both had hip fractures. One, a woman 76 years of age, had a fatal embolus on the fourteenth day after the fracture was pinned, and the other, an 85-year-old man, had a fatal embolus on the fifteenth day after pinning. In both instances the embolus was found to have arisen from a thrombus which formed above the site of ligation.

Treatment and Duration of Life After Massive Pulmonary Embolism.—In most instances the effect of the embolus was so overwhelming that death occurred within 15 minutes, despite emergency treatment with oxygen, heparin, papaverine, aminophylline, and various other means of therapy. Four patients lived for more than 1 hour but less than 24 hours. These patients did not respond to treatment and remained in shock until death. Pulmonary artery embolectomy was attempted in 1 patient. The embolus was successfully removed and the heart temporarily resuscitated, but after beating spontaneously for a few minutes it stopped again and could not be revived.

COMMENT

It is apparent from our experience, which must be typical of that found on the surgical services of many hospitals, that thromboembolic complications still constitute a serious problem in spite of the methods of therapy we have used. Phlebothrombosis or thrombophlebitis occurred in 1 out of 153, nonfatal pulmonary infarction in 1 of 487, and fatal pulmonary embolism in 1 of 896 postoperative patients. Approximately 1 per cent of all postoperative patients had a thromboembolic complication. Since many of the 27,802 patients had a relatively minor operative procedure, the incidence following major surgical procedures was considerably higher. Fatal pulmonary embolism was the cause of 7 per cent of all postoperative deaths during this period.

In an earlier analysis of 67,402 postoperative patients during the period from 1925 to 1944, inclusive, the incidence of fatal pulmonary embolism was found to be about 0.08 per cent (about 1 in 1,200 operations).[1] The higher incidence in the present series is probably due to the more frequent performance of procedures of greater magnitude in a somewhat older age group. Increased interest in thromboembolism problems resulting in more accurate diagnoses and more accurate records are probably contributory factors.

General prophylactic measures, such as using elastic bandages and early ambulation, have not been strikingly successful in our experience, as evidenced by the preceding statistics. Many of the patients who developed phlebothrombosis or thrombophlebitis, 26 of those with nonfatal pulmonary infarction, and 6 of those with fatal pulmonary embolism satisfied the criteria of moderate to full ambulation. In 19 patients with fatal embolism ambulation was not possible because the patients were comatose, too ill, or too debilitated to be out of bed.

The treatment of diagnosed phlebothrombosis, thrombophlebitis, and nonfatal pulmonary infarction by ligation, or with anticoagulants, was successful in

most instances. Three patients with phlebothrombosis had pulmonary infarction following ligation but recovered on heparinization. A fourth had an infarct after unilateral ligation, and a fifth, who was heparinized, had repeated infarcts which stopped after ligation. A massive fatal embolism occurred in a patient who was, we believe, adequately heparinized. In all other instances the patients were free of further complications which suggests that they were adequately protected.

Whether ligation or anticoagulants, used as prophylactic measures, would have spared the lives of many of the patients with fatal pulmonary embolism is, of course, not known. It is known that 4 of the patients who were given the benefit of these measures were not protected. Two had prophylactic bilateral superficial femoral vein ligations, 1 was apparently adequately heparinized, and 1 died 24 hours after heparin therapy was stopped. The principal problem in the patients with fatal embolism was the absence of warning. Specific protective measures could not have been made available to them unless they were used prophylactically in many thousands of patients, or unless the relatively small number of patients susceptible to massive pulmonary embolism could have been detected by some simple, reliable laboratory test.

During the 5 year period under discussion we have followed with interest the experiences of others with the application of mass prophylactic techniques. Allen[2] and his associates have reported the use of prophylactic bilateral superficial femoral vein ligation in 984 elderly patients in whom the risk of fatal embolism was known, from previous experience, to be unusually great. Four patients died of pulmonary embolism. In 2 the emboli originated in the iliac and in 2 in the deep femoral vein. In a "control" series of 984 patients of similar age, sex, and lesion, 37 patients died of pulmonary embolism. By the use of this prophylactic method, therefore, 33 deaths from pulmonary embolism were apparently prevented.

In 1946 and 1947 there was some interest in using this method on our service and a number of prophylactic ligations were done. We were discouraged from continuing this method more widely by the 2 instances of fatal embolism which occurred following prophylactic ligation. Erb and Schumann[3] were similarly discouraged by their experience with prophylactic ligation at the Philadelphia General Hospital. In a series of 100 consecutive patients with hip fractures, bilateral superficial femoral ligation was done in alternate patients. Death from massive embolism occurred in 2 of the 50 ligated patients and in 2 of the 50 not ligated. In addition, nonfatal pulmonary infarction occurred in 7 patients following ligation and in 4 who were not ligated.

Several large series have recently been reported in which anticoagulants have been used prophylactically, and in them there is evidence of protective action against fatal embolism by both heparin[4] and Dicumarol.[5-8] Protection has been obtained at the risk of hemorrhage and in some instances fatal hemorrhage has occurred.[7, 9] While protamine can be used to neutralize the effect of heparin, our experiences with the use of vitamin K_1 oxide in overcoming rapidly the effect of Dicumarol on the coagulation mechanism have been far from satisfactory. We have found ourselves relying more and more on heparin ad-

ministered in one form or another. The cost of this type of therapy is considerable, however. It is to be hoped that some other agent will soon be available which will have all of the advantages of heparin and Dicumarol and none of their disadvantages. Recent experimental studies in our laboratory suggest that it is not necessary to reduce the prothrombin to hemorrhagic levels to obtain protection against thrombosis by Dicumarol therapy.[10]

Simple laboratory tests, sufficiently sensitive to detect early changes in the coagulability of the blood or which will indicate incipient or subclinical thrombosis, have long been sought. A modified prothrombin test has been reported useful by Sandrock and Mahoney,[11] although less encouraging results with this test were reported by McClure and associates.[12] The suggestion of Cummine and Lyons[13] that fibrinogen B and clotting time determinations might be helpful was not confirmed by Kay and colleagues.[14] A recent test proposed by Ochsner, Kay, DeCamp, Hutton, and Balla[15] is based on the determination of the antithrombin and prothrombin levels daily during the postoperative period. In 301 surgical patients it was found that if the antithrombin level remained at 1 to 32 or higher, intravascular clotting did not occur. It was suggested that the circulating antithrombin is alpha tocopherol, and that the administration of alpha tocopherol phosphate and calcium gluconate prophylactically might maintain high antithrombin levels and prevent postoperative thrombosis. The results in the small series reported would appear encouraging but the number of patients so treated must be greatly extended before the real usefulness of this method of therapy can be adequately assessed.

Cullen, Darrow, and Reese,[16] in our laboratories, have attempted to predict incipient peripheral venous thrombosis by using radioactive sodium deposited in the tissues of the foot. Dr. Seymour Kety[17] and ourselves have been satisfied that no important diagnostic aid can be expected from further studies of this type.

So little is known of prothrombin A and B and fraction 5, of their physiologic control, and of their alterations under a wide variety of pathologic disorders, that important aid in therapy can hardly be expected until studies of a more fundamental type are vigorously pursued.

CONCLUSIONS

1. Despite efforts to reduce their incidence, thromboembolic complications occurred in approximately 1 per cent of 27,802 postoperative patients during the 5 year period from Jan. 1, 1945, to Dec. 31, 1949. Phlebothrombosis and thrombophlebitis occurred in 0.65 per cent, nonfatal pulmonary infarction in 0.205 per cent, and fatal pulmonary embolism in 0.11 per cent of these patients.

2. Elastic bandages to the lower extremities, bed exercises, and early ambulation were the principal prophylactic measures employed. The use of proximal vein ligation and anticoagulants was individualized. Instances of failure despite the use of these measures have been cited.

3. It is probable that the incidence of fatal pulmonary embolism can be reduced only by effective mass prophylaxis, by a clearer understanding of the

important etiologic factors causing venous thrombosis, or by the development of tests which indicate incipient thrombosis so that some type of effective therapy can be instituted.

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DIVISION OF THE POPLITEAL VEIN IN DEEP VENOUS INSUFFICIENCY OF THE LOWER EXTREMITIES

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THE number of patients afflicted with postphlebitic sequelae in the lower extremities is very large and difficult to estimate. Postphlebitic sequelae in the lower extremities consist of pain, edema, induration, dermatitis, and ulceration. Perhaps it would not be amiss if we briefly analyzed these symptoms.

PAIN

Pain, in this syndrome, is of 3 distinct types: the first type is causalgic; it is seen in conjunction with cold, clammy, vasospastic extremities which harbor deep venous obstruction. The pain is diffuse, stocking-like in distribution, and is aggravated by nervous tension and emotions. Specifically, it can be eliminated by paravertebral sympathetic block, and if relief is only temporary, by sympathectomy. In our experience, this type of pain is infrequent, and occurred in 5 per cent of our recently reviewed cases. This is in contrast to the conception of Ochsner and DeBakey,[1] who stress the vasomotor element of thrombophlebitis.

The second type of pain courses along the femoral and, more distally, along the saphenous veins. It has a definitely segmental character. When one explores the vascular bundle of the groin, it is seen that frequently the vascular sheath is filled with organized fibrinous exudate which encases the saphenous nerve. In 1937,[2] I reported the case of a nurse in whom the ileofemoral venous segment was stripped of its fibrous envelope and who promptly lost her persistent pain. In saphenous neuritis, when recognized, the nerve can be resected for a distance of 2 to 3 inches. This pain is often responsible for a marked thrombophobia in patients who complain of a painful vein in Hunter's canal, and who are convinced that a new thrombosis has developed.

The third type of pain is the one we are concerned with here. It is the "bursting" type of pain which subsides gradually in the horizontal position and which occurs on standing up after arising in the morning. It is described by the patients as a feeling of tension which can be improved by active muscular contractions for which they like to employ massage. Such pain, together with evidence that a bunch of tortuous, dilated veins fill up suddenly in the erect position in spite of a constricting tourniquet obstructing saphenous backflow, is characteristic of deep venous insufficiency.

EDEMA

Swelling which accompanies the postphlebitic syndrome is either a soft pitting edema which improves or disappears after a night's stay in bed or a hard lymphatic type of swelling which is more persistent and which is accom-

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panied by palpable lymph glands in the popliteal fossa or in the groin. The first type of swelling is obviously due to deep venous insufficiency. The second is the result of the perivenous inflammatory reaction around the thrombosed segment, which in our experience can be readily influenced in the early days of its appearance by roentgen therapy,[3] but for which there is practically no help in the late stages of perivenous fibrosis. It is true that Jennings,[4] in 1933, in describing the "choked" leg, advocated the excision of this perivenous collar for great length, but our experience with this method simply resulted in abolition of the saphenous neuritis with no effect on the edema.

INDURATION

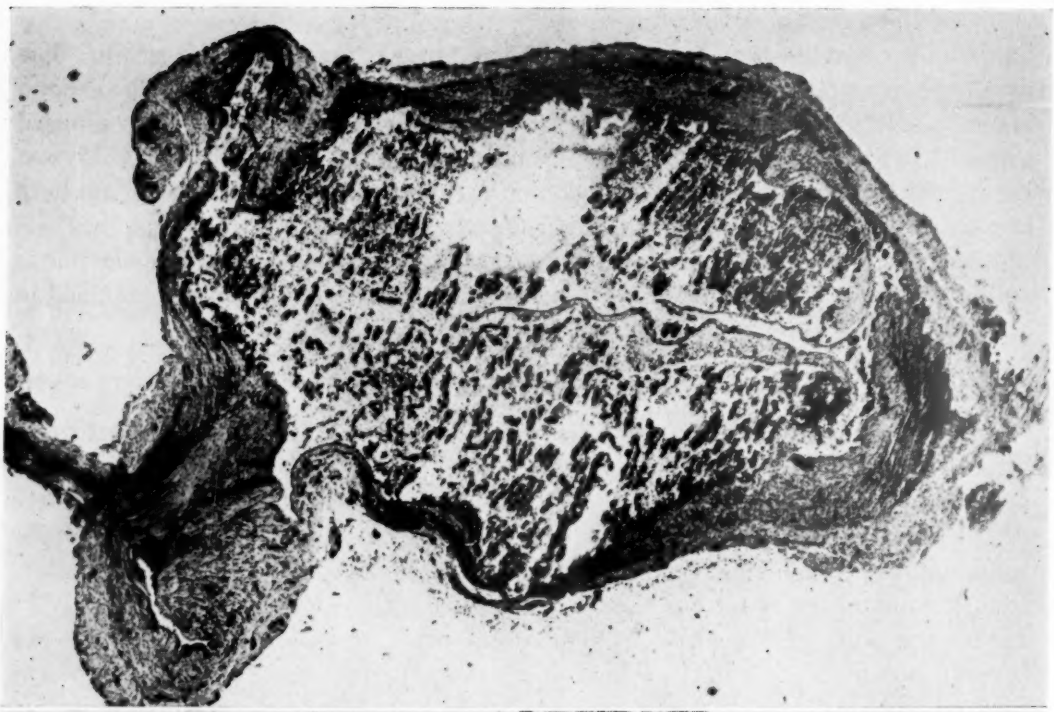
The classical description of this complication was given by Homans,[5] and later its development was traced by Birger.[6] These hard pigmented patches are mostly seen above the inner ankle and sometimes on the posterior surface of the calf. They have a hard scalloped border and are the site of recurrent inflammatory patches of lymphedema and consist of plasma clots, granulomatous inflammatory reactions, and fat necrosis. They may spread centrally as far as the level of the knee. Their center often breaks down and forms the typical postphlebitic ulcer, which heals slowly and recurs readily. While methods of elastic compression are temporarily helpful, and while rest in bed may heal the ulcer, the recurrence rate is very high, and they produce months and years of painful disability for patients afflicted with them. In this group of patients we have employed a wide excision of the induration, if necessary involving the underlying fascia. The defect is then covered, either immediately or better after a short delay, with a split-thickness skin graft. Deep venous insufficiency plays little if any role, although, when excising this mass, one may find a gaping perforator on which the ulcer rides.

It can be seen, then, that the postphlebitic sequelae readily group themselves into 3 forms: (1) the causalgic type with a good deal of pain and frequently hardly any swelling; (2) the lymphatic type with very little pain, few if any varicosities, and a hard nonpitting edema; and (3) the syndrome caused by deep venous insufficiency.

DEEP VENOUS INSUFFICIENCY

Deep venous insufficiency may be of congenital origin and this was particularly emphasized in a small, excellent, but little known monograph by Turner Warwick.[7] One sees this syndrome mostly in young girls who have never had an attack of thrombosis and in whom the early marked postural venous hypertension produces extensive and atypical varicosities. In the last year we have operated upon 5 such patients. The second most frequent group concerns patients who have had a deep venous obstruction due to thrombosis and in whom the thrombus recanalizes, leaving the patient with an insufficient valveless rigid tube, since the valves are destroyed in the process of clot retraction. It is almost impossible to estimate the incidence of recanalization in the deep venous system, but judging from our observation it must be very large (Figs. 1 and 2). The idea that such deep venous insufficiency can be influenced

Fig. 1.



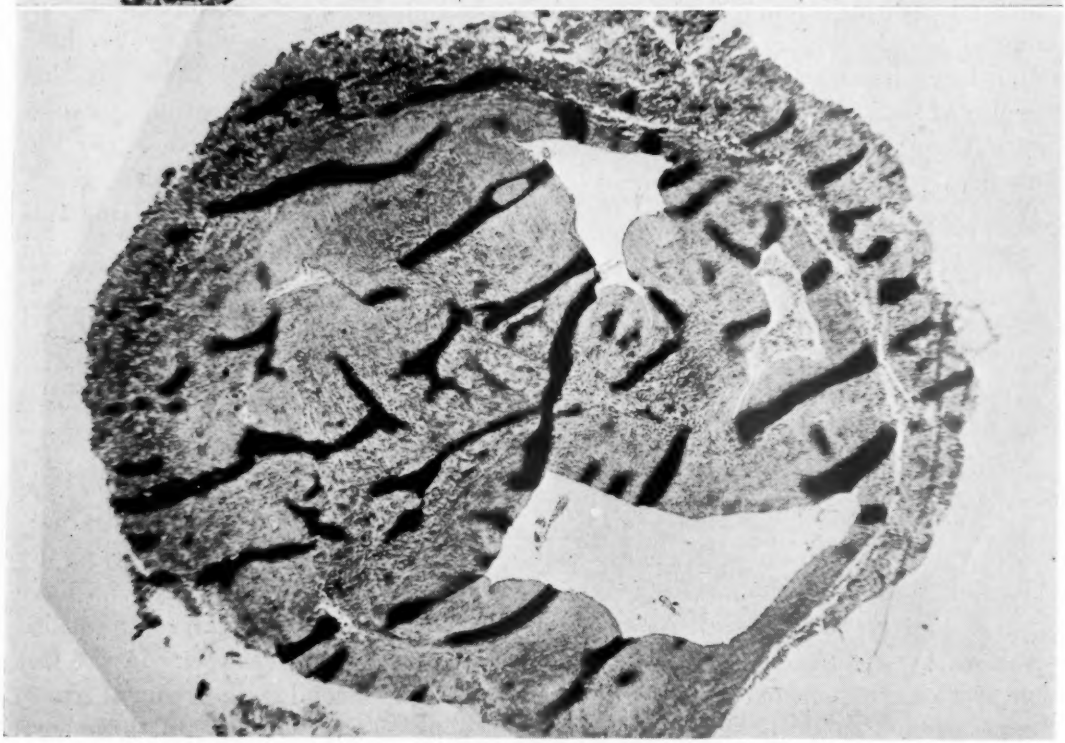


Fig. 2.

Fig. 1.—Recanalized popliteal vein in the case of P. N., whose phlebogram is shown in Fig. 5. This patient gave a clear-cut history of deep venous obstruction and then exhibited symptoms of deep venous insufficiency. Note the thickened intima and the fragmentation of the old thrombus with canalized spaces.

Fig. 2.—Section of the popliteal vein in the case of A. K., a 35-year-old woman who suffered deep venous thrombosis following an automobile accident. On exposure and transsection, the popliteal vein was thickened and showed a definite lumen. The recanalization here seems to be due to clot retraction. There could not have been too much reflux through this vein.

by division of the superficial femoral vein just below the profunda has been promulgated by Buxton, Coller and associates,[8] Linton and Hardy,[9] and more recently by Glasser.[10] The reports emanating from Coller's department were very cautious and conservative, and, in fact, the second report was more pessimistic than the first. Linton and co-workers advocated the simultaneous interruption of the superior femoral and saphenous veins with control by venous pressure measurements.

Our experience with this method in patients who showed deep venous reflux has not been convincing. The edema and pain have not been increased, but there seems to be very little benefit. For this reason we became greatly interested in the reports of Bauer,[11] who advocated on the basis of phlebography and venous pressure measurements the interruption of the backflow at popliteal levels. This procedure appealed to us because femoral vein interruptions do not decrease venous pressure sufficiently in the erect position and because the satellite veins which one sees in the phlebograms of patients affected with deep venous thrombosis still carry blood from the thigh to the popliteal vein in a retrograde fashion.

MATERIAL STUDIED

A study of 100 consecutive records taken from our files of patients suffering from venous involvement of the lower extremities indicates that roughly one-half of them suffered from a postphlebitic syndrome (Table I). This diagnosis

TABLE I. VENOUS INVOLVEMENT IN THE LOWER EXTREMITIES
(100 CONSECUTIVE CASES)

SITE OF LESION	NUMBER OF PATIENTS
Saphenous and perforator incompetence	54
Postphlebitic syndrome	46
Total	100

was based not only on an adequate search for past history, but also on physical findings of collateral patterns and of reflux of blood in the deep venus system when the superficial venous system was occluded by a tourniquet. The tests of Trendelenburg and Perthes were carried out. Palpable or visible collapse of the bulging veins of the calf on muscular exercise with a tourniquet just above the knee meant unobstructed deep venous drainage of the limb. In addition, phlebograms and venous pressure determinations have been carried out, but they are not essential for the diagnosis.

The postphlebitic sequelae which result from deep venous reflux must be distinguished from those which are due to nerve irritation due to scarring, or evidence of lymph block. The latter 2 sequelae cannot be influenced by interruption of the deep veins.

When patients manifest a deep venous insufficiency, their perforator and saphenous valves become incompetent (Fig. 3). This always calls first for high saphenous ligation followed by stripping, which alone may give a great deal of benefit, heal ulcers, and decrease edema. We have advocated this procedure first, before undertaking division of the femoral vein (Table II). Also, many

TABLE II. MANAGEMENT OF POSTPHLEBITIC SEQUELAE WITH DEEP VENOUS INSUFFICIENCY

	NO. PATIENTS
Multiple ligation and stripping	24
Division of popliteal vein	4
Combination of both procedures	2
Stripping, division of popliteal vein and skin graft	4
No surgical treatment	12

patients show large circumscribed patches of thrombophlebitic induration with or without ulcers and they respond after adequate preparation to a wide excision followed by split-thickness grafts. When lymph stasis or such periphlebitic exudates dominate the picture, deep venous interruption will cause disappointment (Cases 2 and 8). The type of patient under discussion has suffered deep venous thrombosis, and has a "bursting" type of pain on

TABLE III. DIVISION OF POPLITEAL VEIN IN 10 PATIENTS (12 EXTREMITIES)

CASE	DURATION OF SYMPTOMS (YEARS)	PREOPERATIVE STATUS	PREVIOUS TREATMENT
1	20	Recurrent phlebitic indurations, massive lymphedema	Bed rest, antibiotics, Unna boots
2	16	Slight edema, saphenous neuritis, resistant ulcerations	Crushing of saphenous nerves, excision of ulcer and skin graft, Unna boots
3	8	Resistant ulceration, large varicosities, causalgic pain	Saphenous vein ligation, superficial femoral vein ligation, vein stripping, excision, and graft
4	20	Recurrent ulceration, huge edema, dermatitis	Casts, bandages, bed rest
5	6	Massive induration upper calf, no saphenous involvement	Unna boots, x-ray therapy
6	25	Induration, ulceration	Saphenous ligation, stripping, and skin graft
7	9	Edema, ulceration, total disability	Bed rest, antibiotics, elastic support
8	4	Painful ulcer, edema, bilateral	Unna boots, bed rest
9	10	Multiple ulceration, edema, total disability	Unna boots, vena cava ligation, right lumbar sympathectomy
10	27	Chronic recurrent ulcer with edema	Stripping, excision of graft

standing, with many varicosities below the knee which cannot be held back by a tourniquet below the knee but will collapse on exercise; his induration or ulceration is chronic and cyanotic, and there is obvious evidence of congestion and stasis-dermatitis. Many years of conservative treatment, including repeated courses of bed rest, fomentation, Unna boots, dermatologic care, and ligation of superficial femoral vein or vena cava, have preceded the therapy under scrutiny (Table III).

TABLE IV. DIVISION OF POPLITEAL VEIN; EFFECTS ON DISABILITY

	NUMBER OF OPERATIONS	RELIEF	IMPROVEMENT	FAILURE
Bursting pain	10	10		
Edema	10	6	2	2
Ulceration	11	7	1	3
Dermatitis	4	4		
Induration	4		2	2

The effect of this operation on disabling symptoms is tabulated in Table IV. The effect on "bursting" pain and healing of ulceration was gratifying. But inflammatory, recurrent lymphedema and induration caused some failures. These, of course, may be intractable in the late or previously ill-treated cases, among which sclerosing injections of postphlebitic varicosities play a conspicuous part. The injection of postphlebitic varicosities greatly adds to the difficulties of management.

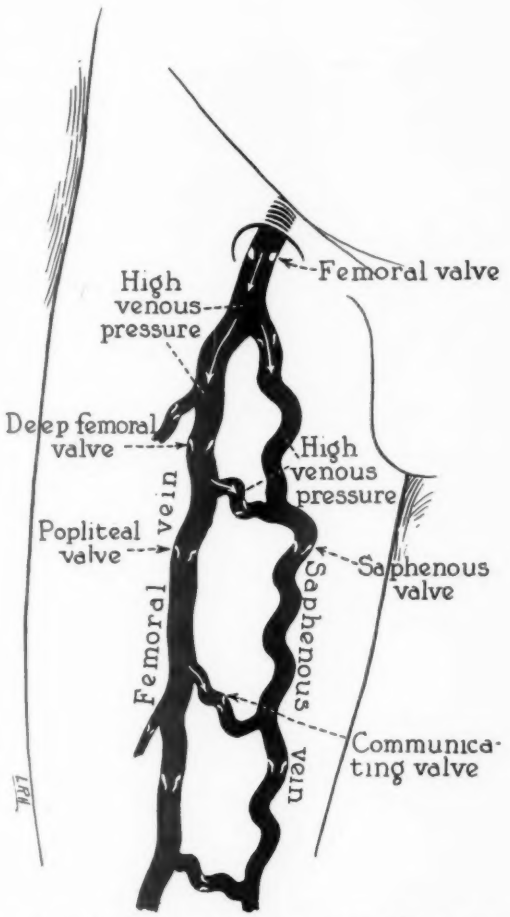


Fig. 3.—Diagram of valvular insufficiency of the superficial perforator and deep veins. One two, or all three of these venous systems may be involved.

DISCUSSION

It should be emphasized that this procedure, which is carried out under local anesthesia and requires no more than 2 to 3 days of hospitalization, should only be undertaken in patients who show evidence of deep venous back-pressure in the erect position as demonstrated by clinical examination or phlebography (Figs. 4, 5, and 6). While venous pressure determinations are helpful in dif-

ferent positions with and without exercise and while we ourselves made such determinations as far back as 21 years ago,[12] we do not believe they are necessary for the clinical evaluation and management of the patient. Obviously, patients with marked lymph stasis or with a causalgic type of pain will not

Fig. 4.—Phlebogram of V. S., 35-year-old man, who had a typical history of deep venous thrombosis with pain and edema in the calf, followed by appearance of large superficial varicosities with many incompetent perforator valves. The visualization with 35 per cent Diodrast shows a large tortuous popliteal vein which can be followed to a supracondylar level. There are a number of tortuous and saccular varicosities as a result of deep venous backflow. This patient is not in the present series, as he has not yet been operated upon.

derive any benefit from the procedure. The result in the properly selected patient has been satisfactory; analysis of the causes of failure in 3 patients of this series has helped to crystalize our indications. In none of the 3 patients was there a typical "bursting" type of pain, or was there demonstrable venous

reflux through the popliteal vein. In a consecutive series of 100 patients with varicosities, we made a diagnosis of the postphlebitic syndrome in 46, and of these divided the popliteal vein in 10. It is possible that the operation was unnecessary in 3 of these, leaving 7 patients out of the 46 who showed demonstrable benefit from this procedure (15 per cent).

Fig. 5.—Phlebogram of P. N., a 51-year-old man, obtained after exposure of the popliteal vein. This patient has had a good history for deep venous thrombosis and showed marked reflux of blood on standing. His popliteal vein was thickened and satellite veins were visible. There seems to be a filling defect at the level of the patella, which may represent a partially recanalized thrombus. A histologic section is shown in Fig. 1.

In previous communications[13] we have expressed considerable doubt as to the advisability of deep venous interruptions in an extremity when venous drainage has already been crippled. We would like to emphasize again that even at the popliteal level the operation can do more harm than good. In fact, there was no need to do anything more than prescribe an elastic hose made to order for 12 out of 46 patients.

The patient who clinically benefits from interruption of the popliteal vein constitutes a small minority of those afflicted with the postphlebitic syndrome. Based on our present small experience he should exhibit (1) visible varicosities on the calf which do not collapse in the erect position in spite of a tourniquet at different levels; and (2) varicosities which collapse on 10 rapid flexions

Fig. 6.—Phlebogram of B. M., a 56-year-old man (Case 10). Here was a clear history of postphlebitic sequelae for 27 years with previous stripping and skin grafting. Films show a large patent popliteofemoral segment.

and extensions of the knee in spite of a tourniquet and which rapidly refill on cessation of exercise while the tourniquet is still in place. The patient, however, who shows no collapse or shows increased filling of veins on exercise suffers predominantly from deep venous obstruction, and we have always advised against any surgical therapy (see Varicose Vein Exhibit, American

Medical Association, 1941) in such a case. In the venous pressure measurements of De Camp and associates,[14] such patients respond with no or minimal fall of pressure during exercise and show a secondary rise in pressure above the resting level on cessation of exercise.

In addition to the congenital and postphlebitic types one finds a third type which is due to a peculiar phlebosclerosis of the popliteal vein. This has been recently studied by Saphir.[15] The vein is sclerotic and thickened, but does not seem to have ever harbored a thrombosis. Its valves cannot close and hence act as a source of postural venous hypertension.

CASE HISTORIES

CASE 1.—A. W., a 52-year-old white woman, was admitted to St. Luke's Hospital on Dec. 28, 1948. She complained of aching and swelling of both legs and ankles, more severe on the right, for over 20 years. In June, 1948, she developed an acute deep thrombophlebitis in the right leg. Conservative therapy for 4 weeks produced improvement, but she complained of "bursting" pain in the right leg. Application of an Unna boot to the right leg produced some relief. She also had had an ulcer on the medial aspect of the lower leg for several weeks, which was now healed. Physical examination revealed swollen and discolored legs and ankles. The lower legs were firm, indurated, and moderately tender. On Jan. 4, 1949, the right short saphenous and popliteal veins were ligated and severed. The popliteal vein was thick-walled and the lumen appeared to be reduced in size. Convalescence was uneventful, and she went home with bilateral Unna boots on Jan. 7, 1949. She was seen a few weeks after surgery and appeared to be relieved of the "bursting" pain. She was lost track of until December, 1949. At this time she exhibited a right leg which was hot, red, tender, and quite indurated. While the "bursting" pain on standing had subsided, the inflammatory lymphedema was not influenced. Roentgen therapy and Unna boots were continued. Treatment in her case was classified a failure.

CASE 2.—F. S., a 53-year-old white woman was admitted to St. Luke's Hospital on Jan. 7, 1949. She gave a history of a right-sided deep phlebitis which occurred 6 years before, associated with typhoid fever. She complained of a feeling of heaviness in the right leg, pain in the calf, and swelling of the foot. No large varicosities were present. Six years ago she had had a "nerve crush" for pain in right leg and ankle. She developed an ulceration over the right medial malleolus 2 years ago. Excision and skin graft at that time healed well. The ulcer recurred in August, 1948, and was present at this time. On Jan. 14, 1949, the right short saphenous and popliteal veins were ligated and severed. There was evidence of chronic phlebitis in the popliteal vein. She was placed on prophylactic heparin for 2 days postoperatively and went home on Jan. 22, 1949, relieved of the "bursting" pain on standing. In March, 1949, the right leg ulcer reopened, although the swelling had disappeared and there was only moderate pain in the leg. A skin graft was placed on the ulcer at this time. She was admitted to the hospital on Oct. 30, 1949, with another recurrent ulcer. On Nov. 3, 1949, a right saphenous vein stripping was done along the entire course of the vein. She developed a pulmonary embolism on Nov. 16, 1949, from a phlebothrombosis of the opposite leg. She was treated conservatively with anticoagulants and recovery was uneventful. She was discharged from the hospital on Dec. 3, 1949; the right leg ulcer was healed; there was no swelling and no pain on walking. Her functional recovery was most satisfactory.

CASE 3.—M. H., a 48-year-old white woman, was admitted to St. Luke's Hospital on Jan. 23, 1949. She had noted some varicosities of both legs for 20 years. She had had recurrent ulcerations over the right medial malleolus for 5 years which could be healed with Unna boots. She gave no clear-cut history of a deep phlebitis. She complained of pain, burning, and itching of the right lower leg. The right leg revealed a superficial ulcer 3 by 5 cm. in size and a leg which was indurated and moderately swollen. The left leg was also indurated and slightly swollen. On Jan. 26, 1949, she had a bilateral popliteal vein ligation and liga-

tion of the right short saphenous vein. The right popliteal vein was large and showed marked chronic inflammatory reaction with dense adhesions to the surrounding tissues. She left the hospital on Jan. 29, 1949, wearing elastic bandages. She was seen a few weeks after the operations. The ulcer was healed, and she stated that she had no pain even though she was on her feet most of the day. In December, 1949, she was seen again. No ulcer or pain and very little swelling occurred in spite of lack of elastic support. She had suffered abrasion at the old ulcer site which healed in 3 days. Her recovery was regarded as excellent.

CASE 4.—R. P., a 20-year-old white man, was admitted to St. Luke's Hospital on May 1, 1949. He had a recurrence of ulceration at the site of a former skin graft to the left inner ankle. This had broken down in February, 1949. He complained of pain and heaviness in the left lower leg. Past history revealed that he had been injured in 1941; he had suffered a traumatic rupture of the spleen which was removed. He then developed a postoperative thrombophlebitis of the left leg which was also contused at the time of the accident. In 1944, he developed an ulceration over the left malleolus with pain and tenderness in the left calf but no prominent varicosities. In 1945 a left high saphenous vein ligation was done, and the ulcer subsequently became smaller but never healed. On Nov. 10, 1947, he had a left superficial femoral vein ligation. The ulcer still refused to heal. On July 25, 1948, he was hospitalized again with throbbing pain in the left leg and enlargement of the ulcer. On July 26 he had a left saphenous ligation and stripping combined with excision of the ulcer on the left lower leg. This area was skin-grafted on Aug. 6, 1948. He had only moderate symptoms after this until February, 1949, at which time the ulcer reappeared with much pain and drainage. On May 11, 1949, he had a left popliteal vein ligation; there was evidence of chronic phlebitis and recanalization of the vein. A razor graft was placed on the ulcer which had been previously cleaned up. Postoperatively he developed an atypical case of scarlatina. He was seen in July, 1949. The ulcer was healed and he suffered none of the previous pain or swelling. He wore an elastic bandage at work. He was seen in November, 1949, with no ulcer or symptoms. In December, 1949, the ulcer was firmly healed. He was doing hard manual labor, without pain and swelling. This case proves the necessity of sometimes combining vein stripping and skin grafting with popliteal vein ligation. The superficial femoral interruption did not seem to interrupt the venous backflow sufficiently.

CASE 5.—R. B., a 44-year-old white woman, was admitted to St. Luke's Hospital on June 16, 1949. She had had varicose veins for many years. Six years ago she had a vaginal hysterectomy and developed thrombophlebitis following this. She suffered recurrent attacks of thrombophlebitis, both deep and superficial, in the right leg. She also showed evidence of increased capillary fragility and had a secondary anemia. She had 6 x-ray treatments for deep phlebitis on the right leg in February, 1949, and wore Unna boots for a few weeks thereafter. She complained of pain and swelling in the right leg and showed an induration and brownish discoloration about the lower leg posteriorly. On June 17, 1949, she had ligation and transection of the right popliteal and short saphenous veins. She has been followed since this operation once a month and has had only slight relief of pain in the leg until December, 1949. Her pain was due to a popliteal neuritis of segmental character. With improvement of the anemia her symptoms improved. The large, almost black, periphlebitic induration softened up and elastic support is only intermittently necessary.

CASE 6.—H. C., a 48-year-old Negro man, was admitted to St. Luke's Hospital on Aug. 16, 1949. He complained of swelling of the right leg since 1924, with heaviness and "bursting" type of pain. He had also had recurrent ulcerations of the medial and lateral right ankle. He suffered from typhoid fever in 1924 and developed a complicating thrombophlebitis of the right leg. He has had intermittent symptoms from the leg as stated previously. He had a high right saphenous vein ligation in 1943 with only temporary relief. In November, 1948, he had a right re-ligation and stripping of a large varicose right saphenous vein and skin grafts to the ulcer. He received relief for several months but the ulcer opened a few weeks prior to present admission. On Aug. 18, 1949, he had his right popliteal and short saphenous veins ligated and severed. Both veins showed evidence of chronic phlebitis and a recanalization

of the popliteal vein was evident. He has been seen at monthly intervals and has complete relief of pain; the ulcer is healed, and only slight swelling occurs if he wears no elastic support.

CASE 7.—P. N., a 62-year-old white man, was admitted to St. Luke's Hospital on Aug. 31, 1949. He had suffered a compound fracture to the left ankle and lower leg 9 years ago. Three years ago he noticed some swelling of the left ankle in late afternoons. He also developed an ulcer on the medial aspect of the left lower leg 3 years ago which has healed and reopened several times. He has also had a "bursting" pain quite severely for the past 3 years which becomes more severe on walking. On admission he had an ulcer on the medial aspect of the lower leg with a chronic weeping dermatitis extending over the entire lower leg. This lower leg was also moderately swollen. He exhibited incompetent long and short saphenous veins on the leg with marked superficial varicosities. After 10 days of bed rest with elevation and warm foments, the skin of the lower leg cleared considerably. On Sept. 9, 1949, a left popliteal short and long saphenous vein ligation was done. There was evidence of chronic phlebitis. A venogram was done at the time of the operation. He was discharged Sept. 13, 1949, with almost complete relief of pain and swelling and marked improvement in the dermatitis. The ulcer was also healed. He was seen in December, 1949. He had no pain, the leg was not swollen, and the skin was intact over the entire leg except for pigmentation. He works a full 8 hours on his feet and has no symptoms.

CASE 8.—A. K., a 29-year-old white woman, was admitted to St. Luke's Hospital on Oct. 9, 1949. She complained of recurrent ulceration about both internal malleoli and a heavy "bursting" pain in both legs from 4 years. She was involved in an automobile accident 4 years ago, during which time she suffered multiple injuries to both legs but no fractures. She was in bed for several weeks. On getting up she noted swelling of both legs and pain. She injured both ankles a short time after this and developed ulceration at both internal malleoli. She has worn Unna boots, elastic bandages, and elastic hose to heal the ulcers and has obtained relief of swelling and heavy "bursting" pain. On Oct. 10, 1949, the right popliteal vein was ligated and on Oct. 12, 1949, the left popliteal vein was ligated. There was evidence of bilateral chronic phlebitis and recanalization. She was discharged Oct. 19, 1949, wearing bilateral Unna boots. She was seen several times in December, 1949; all ulcers were healed and no pain was present. Only slight swelling occurred when no elastic support was worn. In May, 1950, she was re-examined because of recurrent ulceration which needed grafting. However, there was no edema, even without elastic support.

CASE 9.—W. J., a 57-year-old white man, was admitted to St. Luke's Hospital on Feb. 4, 1950. He presented swollen legs with small painful ulcerations over all 4 malleoli. The largest of these was on right lateral malleolus. He had had this swelling and ulceration for 6 months. He also complained of aching and "bursting" pain in both legs for 6 months. The right leg was warmer than the left, and did not sweat. In January, 1948, he had a pelvic thrombophlebitis with thrombosis of the vena cava. A ligation of the vena cava and a right lumbar sympathectomy were done at another hospital. After a period of bed rest, during which time the swelling subsided for the most part, bilateral popliteal vein ligations were done on Jan. 24, 1950. A venogram of the right leg was taken; this revealed open and incompetent popliteal and superficial femoral veins. A small skin graft was placed on the right lateral malleolus. Gelatin casts were applied to both lower legs, and he was discharged from the hospital. He was seen monthly for 3 months with no swelling and only slight pain. The ulcers were all healed.

CASE 10.—B. M., a 56-year-old Negro man, was admitted to St. Luke's Hospital on Jan. 28, 1950. He had a deep thrombophlebitis of the right leg in 1923, following an appendectomy, followed by varicosities. Six years previous to admission he developed an ulcer over the right medial malleolus. This ulcer has healed, and recurred several times since, with conservative treatment. He had a right high saphenous vein ligation in 1944. No improvement followed. A split skin graft was applied to the excised ulcer area in September, 1948. This area remained healed up to several months before present admission. At this time

a recurrent ulcer at the superior border of the grafted area presented itself. He also complained of heaviness of the leg and moderate "bursting" type of pain, unless he wore an elastic hose. A venogram of the right leg was made, revealing a recanalized popliteal and superficial femoral vein. A right popliteal vein division was done on Feb. 1, 1950. The ulcer healed shortly thereafter. Pain and heaviness were relieved. He continued his work as a manual laborer. He died 2 months later from coronary occlusion.

SUMMARY

Types of postphlebitic sequelae have been discussed. Attention has been called to causalgic and lymphatic types of syndromes, and a third one produced by deep venous insufficiency. The deep venous insufficiency can be due to a congenital absence of valves, to a recanalization of thrombi, or to phlebosclerosis. The division of the popliteal vein in cases of deep venous insufficiency has been carried out. Seven patients had excellent results, 3 poorly selected patients had none. Further studies of this disabling malady are indicated.

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ACUTE MASSIVE VENOUS OCCLUSION OF THE LOWER EXTREMITIES

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IT HAS long been recognized that thrombosis of the veins of an extremity occasionally causes grave disturbances in the entire circulation of the limb. The blood flow may be so greatly impeded that gangrene of the toes and feet results. Such serious local circulatory arrest also presents a grave prognosis for life as well as limb. Most of the reported cases have presented similar signs and symptoms. Acute onset with extreme pain, cyanosis, venous congestion, edema, and circulatory failure of the involved extremities are the cardinal manifestations. The exact cause of such complete local circulatory derangement has not been settled. Arterial spasm has frequently been emphasized as the most important vascular disturbance. In some there has been strong evidence of vasospasm, but even these have shown congested veins, blue discoloration of the skin, and edema, which are signs of vascular engorgement. Various terms have been used to describe this condition, such as blue thrombophlebitis or phlegmasia cerulea dolens,[1] gangrene of venous origin,[2] and gangrene from arterial spasm in phlebitis.[3] The essential pathology is an acute and almost total obstruction of the venous bed of the extremity. We feel that the term acute massive venous occlusion should be applied to this entire group.

The paucity of the reports indicates that this condition is rare indeed. However, we feel that many more cases occur than are reported. In some there is undoubtedly a mistaken diagnosis because the patients are not carefully observed in the early stages, when the true nature of the pathology can be recognized, but are seen only in the end stage of gangrene. Furthermore, there is seldom careful dissection of the arterial system of an amputated extremity and the actual cause of the gangrene may not be recognized.

DeBakey and Ochsner[4] presented before this Society 2 years ago an excellent review of this subject. They were able to collect only 56 cases from the recent medical literature. They added 2 of their own and presented their clinical records. In 1, gangrene developed in several toes and amputation was necessary. In the other case they prevented this end result by the removal of the venous thrombus and ligation of the femoral vein. They discussed very thoroughly the clinical picture, the pathogenesis, and the possible explanations of the collapse of the circulation. They concluded that vasospasm is probably responsible in great measure for the pain. They stated further, "The fact, however, that the severe type of venous thrombosis may continue to progress to

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actual gangrene in spite of vigorous antivasospastic measures and the transient improvement produced by them seems to indicate that vasospasm does not play a primary role in the genesis of this condition.'' They feel that the most plausible explanation is a simple blockage of the circulation by the thrombosis.

We have now had 11 cases of acute massive venous occlusion involving 1 of the lower extremities. Our observations on these, with a description of their management, and some data on experimental acute venous obstruction, form the basis of this report. The recent articles by DeBakey and Ochsner[4] and Haimovici[5] make it unnecessary for us to include a review of the previous reports.

All of our cases have presented a similar clinical picture with some variations in intensity and duration of the symptoms.

In Table I we have listed the cases with the etiology, limb involved and the results obtained in each instance.

TABLE I. ACUTE MASSIVE VENOUS OCCLUSION

CASE	ETIOLOGY	EXTREMITY INVOLVED	RESULTS
1	Postpartal thrombophlebitis	Left lower	Gangrene; amputation
2	Postpartal thrombophlebitis	Left lower	Recovered
3	Acute massive chemical thrombosis	Right leg	Gangrene; amputation
4	Phlebothrombosis, shifting thrombus	Left lower	Recovered
5	Phlebothrombosis, shifting thrombus	Left lower	Recovered
6	Phlebothrombosis, shifting thrombus	Left lower	Recovered
7	Left thrombophlebitis, vena caval ligation	Right lower	Recovered
8	Right phlebothrombosis, external iliac ligation	Right lower	Recovered
9	Left phlebothrombosis, femoral vein ligation	Left lower	Recovered
10	Right phlebothrombosis, femoral vein ligation	Right lower	Recovered
11	Left phlebothrombosis, vena caval ligation	Right lower	Recovered

The first postpartal patient presented a typical femoroiliac thrombophlebitis. Several days after onset she suddenly developed the cardinal signs of acute massive venous occlusion. The pain was extreme, the venous engorgement prominent, the skin became deeply cyanotic, and this discoloration extended well upon the thigh. The swelling increased rapidly. The extremity was cooler than the opposite member and the pulses of the foot were markedly diminished. Repeated lumbar sympathetic blocks failed to relieve the pain or re-establish the blood flow. Improperly, heat was applied and the leg was immobilized. The end result was gangrene of the toes and foot (Fig. 1). The leg was amputated just above the knee. Dissection of the extremity showed that every visible vein was thrombosed. The arterial system was patent throughout.

The second postpartal patient presented a pseudoembolic episode. A diagnosis of arterial embolism had been made. On examination we found a cold, blue, excruciatingly painful extremity. The pulses of the foot were absent.

The entire limb was moderately swollen and the superficial veins were distended. The femoral vessels were explored in the femoral triangle and the true nature of the condition was found. She presented an acute femoroiliac thrombophlebitis. The femoral artery was constricted but a pulsation could be demonstrated. A periarterial sympathectomy was performed and shortly a lumbar sympathetic block was also done. These measures gave some relief of pain but the signs of venous congestion persisted. The leg was placed high on soft pillows and active and passive motion was started. The color rapidly returned and the pain quickly subsided. She recovered without further incident.

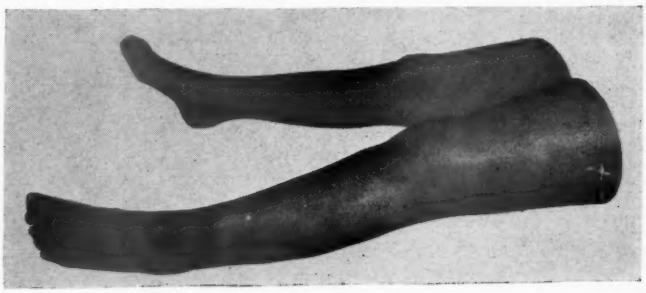

Fig. 1.—Gangrene of the foot following acute massive occlusion of the veins of the left lower extremity. The occlusion occurred some days after onset of acute postpartal femoroiliac thrombophlebitis.

One of us (J. R. V.) was consulted on a case of gangrene of the foot and lower leg that followed the injection of a sclerosing solution in the treatment of varicose veins. The saphenous vein had been ligated in the groin and 10 c.c. of the sclerosing agent injected through a catheter into the veins of the leg. Almost at once the patient had complained of severe pain in the entire limb. The foot and leg became blue and cold. The patient was seen 36 hours later and the foot and leg were still cold and blue. The entire extremity was swollen. The pulses of the foot were absent. Repeated lumbar sympathetic blocks produced no increase in blood flow, nor did they relieve the pain. At amputation, above the knee, both the superficial and deep veins were thrombosed. The arterial system was entirely free from clots.

The 3 remaining cases of massive venous occlusion, occurring in patients with venous thrombosis, presented a different series of events. The massive occlusion followed the sudden plugging of the femoroiliac veins by a thrombus shifting upward from the deep veins of the legs. Each of these patients was known to have phlebothrombosis of the deep veins of the leg which probably extended into the popliteal and lower femoral veins. There was no evidence of higher obstruction. In each there was a sudden onset of pain in the groin and lower abdomen and shortly an engorgement of all of the veins of the involved limb. The extremity became excruciatingly painful, discolored, and began to swell rapidly. Two were such striking cases that a short history seems indicated.

A 60-year-old man had a right hip fusion performed on April 30, 1947, and was placed in a hip spica cast. The immediate postoperative course was uneventful. Some swelling of the left leg was noted on the tenth postoperative day. On the fourteenth

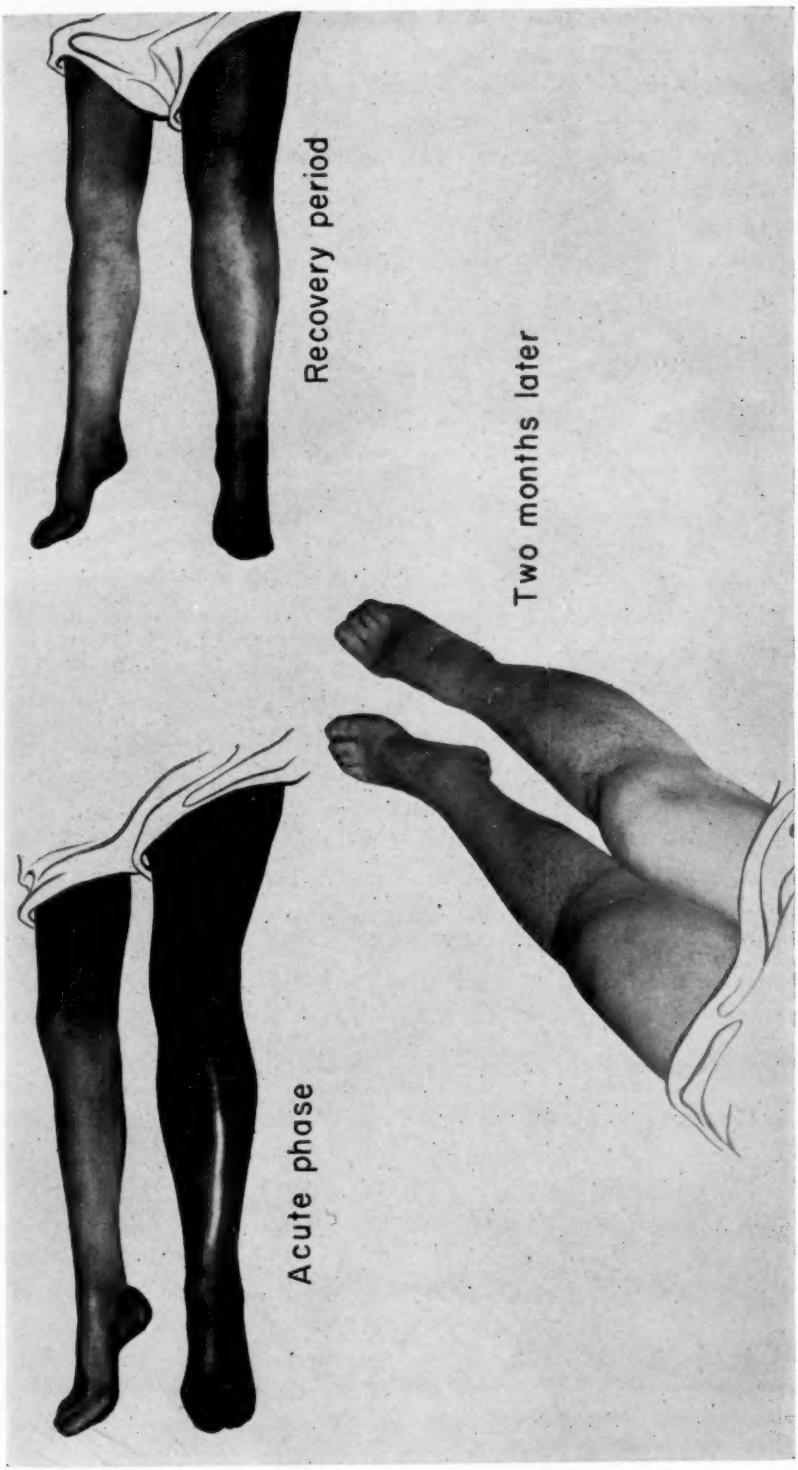

Fig. 2.—Acute massive occlusion of the veins of the left lower extremity. The occlusion was caused by a sudden plugging of the major veins by a shifting thrombus. There was complete recovery.

postoperative day he developed sharp pain in the lower abdomen and left groin. Suddenly he experienced an acute, excruciating pain in the entire left lower extremity. The house officer was called immediately and he found that the left foot and leg were blue and that the superficial veins were engorged. The dorsalis pedis and posterior tibial pulses seemed normal. The discoloration deepened and extended upon the thigh. The pain became more intense and was not relieved by morphine. The extremity began to enlarge rapidly and petechial hemorrhage in the skin was noted. A lumbar sympathetic nerve block (Novocain 1 per cent) was done with little relief of pain. A second block was performed with only slight results. About 4 hours after onset the symptoms were still serious. At this time Novocain in oil was instilled in the region of the lumbar chain. Even this did not relieve the pain but did bring about an even more serious condition. The leg showed a rapid increase in swelling and seemed that it would burst. The limb was then elevated and exercises promptly instituted. The color improved and the pain subsided. About 4 hours later the patient's blood pressure began to decline and soon reached the shock level. The blood pressure was restored by a blood transfusion. Urinary output decreased and only 300 c.c. was excreted in the next 24 hours. Nonprotein nitrogen reached 215 and the creatinine 4.5. The renal failure cleared in a few days under appropriate treatment. The swelling of the extremity gradually subsided but had not completely disappeared at the time of his discharge on July 6, 1947. By sweat tests it was apparent that the Novocain in oil had caused a block of the sympathetics that lasted approximately 4 weeks.

The second case was that of a 52-year-old white woman who was admitted to the hospital with a fracture of the seventh dorsal vertebra. There were no abnormal neurological signs. Two weeks after admission she developed phlebothrombosis of the deep veins of the left leg. Several days later she suddenly developed pain in the lower abdomen and entire left lower extremity. The pain was so acute and intense that it was almost unbearable. The entire limb became deeply discolored and began to swell rapidly. The deep purple color was strikingly uniform (Fig. 2) and extended from the tip of her toes to the groin. The pulses of the foot were palpable. The superficial veins were engorged. An immediate sympathetic nerve block was performed without relief. The limb was then elevated quite high and vigorous exercises were started. The foot was flexed and extended and at the same time the leg was similarly exercised. The response was prompt. The pain began to subside and the color gradually improved. Throughout the day (some 8 hours) the exercises were continued. At this time it was evident that the circulation had been re-established. She recovered completely except for moderate persistent edema of the leg.

Our first experience with the syndrome of acute massive venous occlusion from venous surgery followed the ligation of the vena cava. This was a case of thrombosis of the deep veins of the left lower extremity. The thrombus had extended up to the vena cava. Because of repeated episodes of pulmonary embolism the vena cava was ligated. The operation was performed under spinal anesthesia, but the spinal lasted only 30 minutes and the operation was completed under intravenous pentothal. Upon completion of the operation the patient awakened promptly. It was noted that the veins of the normal right leg and foot were markedly engorged and there was cyanosis of the toes and foot. The pulses were intact. About 15 minutes after leaving the operating room the patient began to scream with intense pain in the right leg and thigh. Examination revealed an increasing cyanosis of the entire right lower limb. The superficial veins were markedly distended and the extremity began to swell rapidly. Small petechial hemorrhages were noted over the entire limb. The pain was so intense that it was difficult to keep the patient in bed. A lumbar

block was performed at once with some relief of pain; however, the cyanosis and swelling were not relieved. At this stage the patient's blood pressure began to decline and the pulse became rapid. It was obvious that he was losing a large amount of fluid into the tissues of the limb. The leg and thigh were elevated to about a 60 degree level and rapid exercise of the foot and leg were initiated. There was steady improvement. The pain subsided, the cyanosis disappeared, and the veins became less engorged. A blood transfusion restored the blood pressure. His recovery was uneventful and only the residual edema commonly seen in the postphlebitic patient persisted.

The 4 remaining cases that followed ligation of a major vein in the treatment of venous thrombosis presented a similar picture. Shock developed in only 1 instance. In 1 the vena cava was ligated for recurrent embolism from acute thrombosis of the deep veins of the left lower extremity. The thrombus had filled the left iliac veins and had reached the vena cava. On ligating the vena cava the right limb, which did not contain a thrombus, became acutely engorged and rapidly developed all the signs of massive venous occlusion. The other cases resulted from ligation of the external iliac in 1, and the femoral below the profunda in 2. In each there was a pre-existing thrombosis of the deep veins of the leg. In all of these a prompt lumbar sympathetic block was performed without relief of symptoms. Only when the limb was elevated and vigorously exercised were we able to restore the blood flow. All in this group recovered without loss of tissue.

The cardinal signs and symptoms of acute massive venous occlusion were present in each of these 11 cases. Acute, excruciating pain was the dominant symptom. The onset of the pain was sudden. The patients usually stated that the entire limb seemed to be expanding as if it were being blown up. Swelling was a constant sign but there was considerable variation in the degree in the several cases. In some, such large quantities of fluid were lost into the tissues of the extremity that systemic shock developed. Blood transfusions quickly restored the blood pressure. Venous congestion was present in every case. In each the limb showed marked discoloration or cyanosis. In some the entire extremity quickly took on a deep purple color. In others the appearance was more mottled and deep gray in color. Petechial hemorrhages were often seen. The involved extremity always showed a decline in skin temperature. The dorsalis pedis and posterior tibial pulses were usually present but did show diminishing volume.

EXPERIMENTAL VENOUS OCCLUSION

Attempts to reproduce massive occlusion of the venous system of the hind limb in the dog presented considerable difficulty. By multiple ligations of the major veins including the vena cava, iliac, and femoral veins, we did produce marked venous congestion, bluish discoloration, lowering of the skin temperature, and an extreme elevation of the local venous pressure. On the following day the extremities showed only edema and dilated superficial veins. All of the extremities recovered completely without developing gangrene. Fontaine and Pereira[6] have shown that gangrene could be produced in animals only when all of the venous return was completely blocked.

The circulation of the mesentery and small bowel provides an excellent arrangement to study the effect of massive venous occlusion. Here it is possible to obstruct the entire venous return and keep the arterial system intact. Ligation of the vein at the root of mesentery leads to extreme venous engorgement, deep cyanosis of the bowel, edema, infarction, and gangrene. If the venous obstruction is released while the tissue is still viable it will return to its normal state.

In order to study more closely the effect of massive venous occlusion upon the arterial blood flow we performed the following experiment.

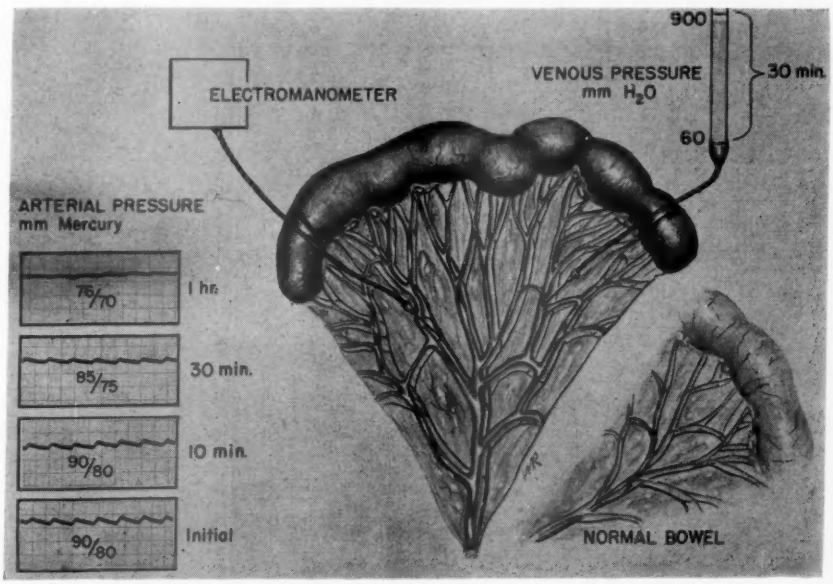

Fig. 3.—The arrest of circulation by complete obstruction and acute massive occlusion of venous blood flow in mesentery of a dog. Note that the arterial system remains patent after venous pressure reaches its peak. Pulsations are transmitted to the arterial system after blood flow has been arrested.

A mongrel dog weighing 25 pounds was heparinized, and anesthetized with morphine and Nembutal. An endotracheal tube was inserted and even respiration was maintained throughout the experiment. The small bowel was delivered through a long midline incision. A segment of bowel measuring about 2 feet was isolated, keeping intact its mesentery with the main superior mesenteric artery and vein. This arrangement made it possible to obstruct the entire venous return flow by a single ligature around the mesenteric vein at its base. The artery and vein at the root of the mesentery were exposed. All other possible routes of exit were ligated. We then cannulated an arterial branch near the gut, using a 25 gauge needle. This was attached to an electromanometer and the pressure recorded. Using this type of manometer we could make continuous tracings of the arterial pressure and record the amplitude of the pulse waves. A corresponding vein of the mesentery was then cannulated and the needle attached to a venous pressure apparatus (Fig. 3).[3] The initial arterial pressure and initial intravenous pressure were recorded. The arterial pressure was 90/80 mm. Hg, the venous pressure 60 mm. water. The mesenteric vein

was then ligated and continuous pressure recordings were made. The venous pressure began to rise steadily. The arterial pressure and pulse volume remained quite constant. In a few minutes the bowel began to take on a purple color, and the mesenteric veins became engorged. At the end of 30 minutes the bowel was very dark in color and veins were markedly engorged. The venous pressure had reached 850 mm. water. The arterial pressure had declined very slightly, the pressure being 85/75 mm. Hg. The pulse volume showed very slight decline. At 1 hour the venous pressure was 865 mm. water. The arterial pulsations were hardly demonstrable. The arterial pressure was 76/70 mm. Hg. The bowel was deep purple, edematous, and petechial hemorrhages were present throughout the mesentery. This experiment produced the cardinal signs seen in the group of patients who presented massive venous occlusion. The arterial system remained open and spasm did not develop. The blood flow came to a standstill when the venous pressure reached its peak. The only chance for arterial blood to enter was in the replacement of the fluid that was being lost into the tissue.

THERAPY

The effects of occlusion of the venous channels of an extremity depend not only upon the amount of venous bed that is blocked but also upon the suddenness with which it develops. A slow obstruction usually allows time for adequate collaterals to form so that a serious overloading is prevented. If the obstruction is sudden and sufficiently widespread irreparable damage may occur before collaterals can develop spontaneously. The veins of the lower extremities present a pattern of varying-sized intercommunicating channels that join with the superficial and deep veins of the lower abdomen. This network of veins also presents variations in size and in distribution. In some the superficial veins and communicating branches are small and relatively unimportant as channels for returning the great volume of venous blood. In this type of arrangement sudden occlusion of the major deep veins may be sufficient virtually to block the entire blood flow. Such an occlusion may result from extensive thrombosis, a shifting thrombus, or from ligation of the major veins. Fortunately, there almost always remain some patent venous channels in the extremities regardless of the type of obstruction. These channels can be made to empty large quantities of blood from the extremities. Sympathetic nerve blocks, although performed early in 9 cases, failed to give relief of symptoms. In our first case we did not attempt measures to express the blood from the limb, and gangrene resulted. In 1 case in which chemical thrombosis caused the obstruction we did not see the patient before gangrene was evident. The remaining 9 cases all responded to elevation of the limb and exercise, which relieved the venous engorgement. The method is simple and we have found it to be safe even in the case in which a shifting thrombosis had caused the occlusion (Fig. 4). The involved extremity has been elevated quite high, from 60 to 75 degree angles. Then the foot has been extended and flexed rapidly. These movements contract and relax the various muscles of the leg and massage the blood upward in the patent veins. At the same time the thigh is flexed and

extended. This contracts and relaxes the thigh muscles and expresses the venous blood forward into the veins of the groin and lower abdomen. When the venous engorgement has been reduced, fresh arterial blood can then enter the vascular bed. As soon as the blood once again begins to flow through the extremity the acute symptoms disappear. The pain rapidly subsides, the cyanosis gradually disappears, the veins show less distention, and the skin temperature becomes elevated. The exercise should be continued with short intervals of rest until the limb can be allowed to remain at a high level on pillows without showing a return of venous engorgement. When this much improvement has been achieved the patient can usually maintain it by actively going through these movements

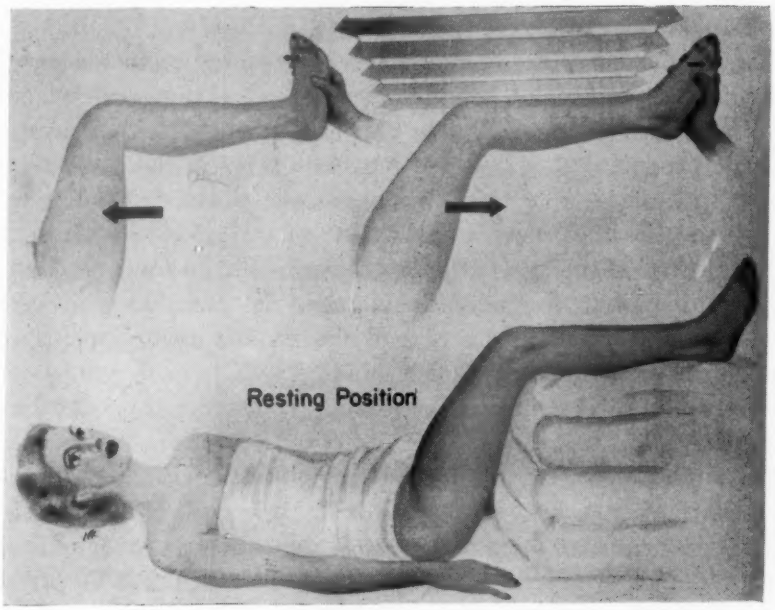

Fig. 4.—Method of expressing venous blood from limb by elevation and exercise of the extremity Exercise to empty overloaded venous system of the lower extremity.

at regular intervals throughout each day. We have maintained elevation of the extremities until all swelling has subsided and have gradually allowed dependency and activity. All patients have been fitted with elastic stockings and are instructed to wear them as long as the edema persists.

In one of DeBakey's cases he was able to open up sufficient pathways by removing the thrombus. This method may prove to be as efficient as the method we have used. Removal of the ligature in the postsurgical cases may at times be feasible and should relieve the obstruction immediately. Anticoagulant therapy does not remove the obstruction and should not be used until the blood flow has been re-established.

SUMMARY

1. Acute massive venous occlusion of a lower extremity may result from extensive thrombosis, sudden plugging of the major veins of the pelvis and thigh by a shifting thrombus, or by ligation of the main venous channel.

2. Eleven cases of acute massive venous occlusion of one of the lower limbs are reported.

3. The local clinical manifestations are acute excruciating pain, cyanosis with extreme tissue anoxia, marked venous congestion, rupture of the capillary vessels, and rapid swelling of the limb. The skin temperature declines. The pulse volume gradually diminishes until there is a complete arrest of the circulation. Unless the blood flow is rapidly re-established gangrene is inevitable.

4. In acute massive venous occlusion there is practically a complete blockage of the venous blood flow. The arterial current continues until the vascular bed is filled to its limit. When this is accomplished we have a condition in which too much blood produces a problem as serious as an arterial embolism in which there is too little blood.

5. The symptom complex of acute massive venous occlusion can be reproduced experimentally only by complete occlusion of the local venous system.

6. Arterial spasm of some degree may occur when there is a strong vasospastic irritant present, but it is not the prime factor in the genesis of the local circulatory failure. Blockage of the venous outlet prevents fresh arterial blood from entering and the blood flow is arrested.

7. Interruption of the sympathetic pathways to the involved limb does not relieve the symptoms but may actually increase the vascular congestion.

8. Measures that diminish or relieve the venous engorgement will restore the circulation of the involved limb.

9. A method of overcoming the vascular congestion by extreme elevation and rapid exercises of the limb has been presented.

10. This method has proved effective in 9 consecutive cases of acute massive venous occlusion of the lower extremities. By prompt institution of these measures a serious catastrophic condition can be rapidly converted into a minor problem.

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AMBULATORY VENOUS PRESSURE STUDIES IN POSTPHLEBITIC AND OTHER DISEASE STATES

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IN A previous report[2] we reviewed some of the pertinent literature, and recorded observations of the ambulatory venous pressure pattern in the lower leg of normal individuals, of patients exhibiting the postphlebitic lower leg syndrome, and of individuals in whom either the inferior vena cava or one of the deep veins of the leg had been ligated.

We have continued the use of the simple method therein described, which consists of the insertion of a large bore (internal diameter 1 mm.) flexible polyethylene tube into a subcutaneous vein of the foot or lower leg. This is then connected with a flexible citrate-filled water manometer system by means of which rapid changes of pressure may be readily observed. Observations are made of the pressure in the pedal vein with the patient resting in the recumbent and in the erect positions, and of the changes in pressure incident to a moderately vigorous "standing walk," lifting both feet 15 cm. 60 times a minute.

In our initial study of 11 apparently normal individuals 10 subjects exhibited the classic pattern of a rapid extensive fall in pressure (Fig. 1), persisting throughout prolonged ambulation, followed by a slow rise in pressure on cessation of exercise. The degree of fall ranged from 50 to 90 per cent with a mean of 66.4 per cent. The postambulation rise in pressure required from 23 to 40 seconds with a mean of 33 seconds. In the eleventh individual, although a rapid and extensive fall in pressure occurred on ambulation, a rapid rise in pressure on stopping exercise, even with compression of the superficial veins, indicated an unsuspected incompetency of the valves of the deep veins.

Patients with uncomplicated severe venous obstruction (ligation of the inferior vena cava for septic pelvic thrombophlebitis) were studied, and they revealed, as typified in Patient H. M.(Fig. 2), a pattern of a slow and reduced fall in pressure initially on ambulation frequently followed by a secondary rise during continued ambulation, presumably due to increased blood flow entering the venous system incident to exercise. On cessation of exercise the pressure rose immediately to above the resting erect level, the excessive rise again apparently due to the influx of blood associated with exercise. It was felt that this secondary rise during ambulation, and the rise above the resting level on cessation of exercise, could be due only to a high grade of venous obstruction.

Among 15 individuals exhibiting the postphlebitic syndrome 4 had patterns indicating a similar high degree of venous obstruction. In the remaining 11 individuals (Fig. 3) a slow and restricted fall in pressure occurred on

Read at the fourth annual meeting of the Society for Vascular Surgery, San Francisco, Calif., June 25, 1950.

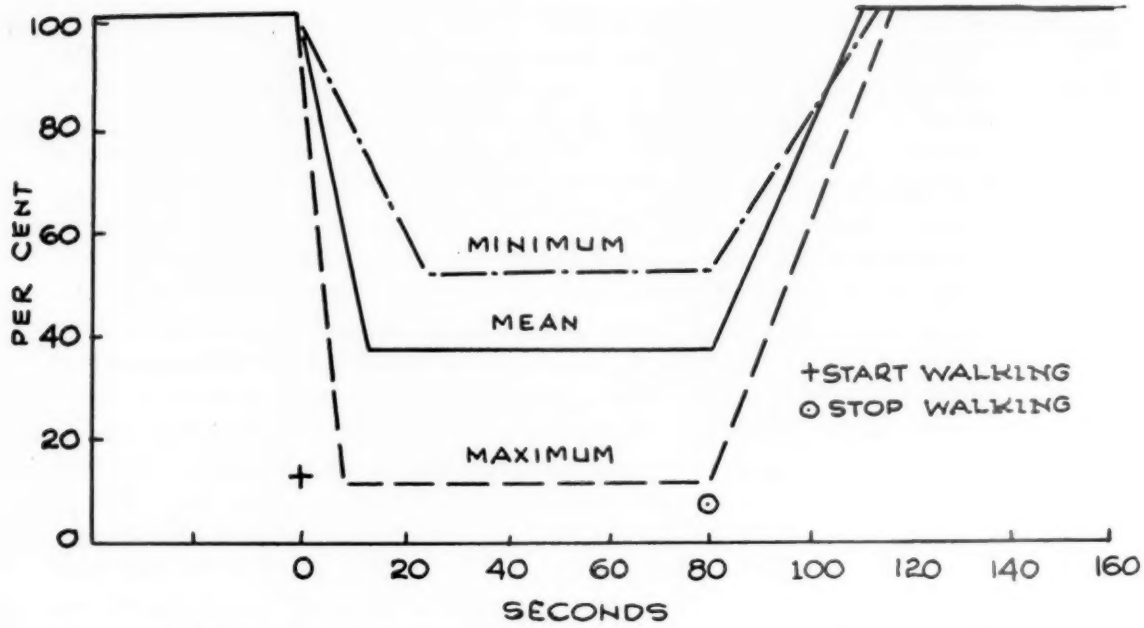

Fig. 1.—Ambulatory venous pressure patterns observed in 10 normal individuals. Maximum, minimum, and mean degrees of pressure fall are indicated.

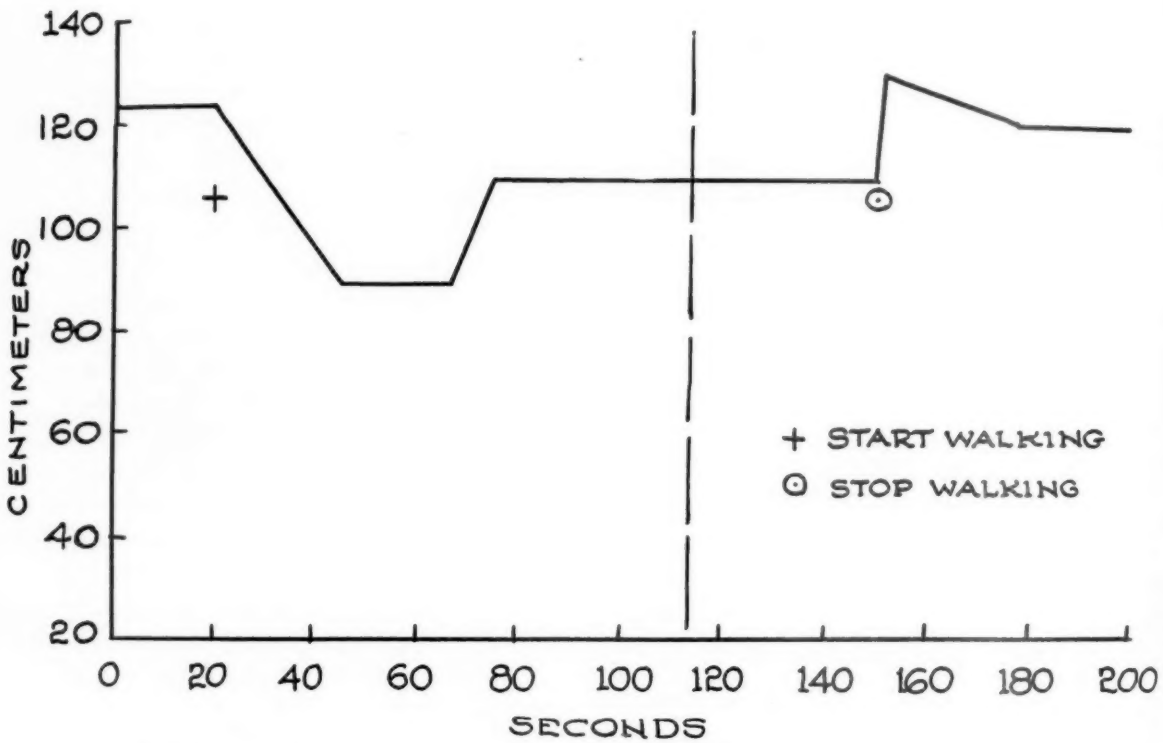

Fig. 2 (Patient H. M.).—Ambulatory venous pressure pattern 12 days after inferior vena cava ligation for suppurative pelvic thrombophlebitis. Minimal edema of the leg present. Evidence is present of a severe degree of venous obstruction.

ambulation and persisted unchanged during prolonged exercise. A sharp rise in pressure occurred on cessation of walking, the pressure returning directly to the resting level. It was felt that these changes could be due either to venous obstruction, to regurgitation associated with valvular incompetence, or to a combination of the two. Comparison of the ambulatory venous pressure pattern and the resting pressures with the patients either erect or recumbent confirmed the thesis of Veal and Hussey[11] that the resting venous pressure is an inadequate index of the presence of venous obstruction. The blood flow in an extremity at rest is not great but is multiplied many times during exercise. A venous outflow tract competent to handle the volume of blood flow at rest is frequently unable to handle the greater volume of flow incident to exercise. This also explains the increase in edema which occurs with exercise in individuals with high grade venous obstruction.

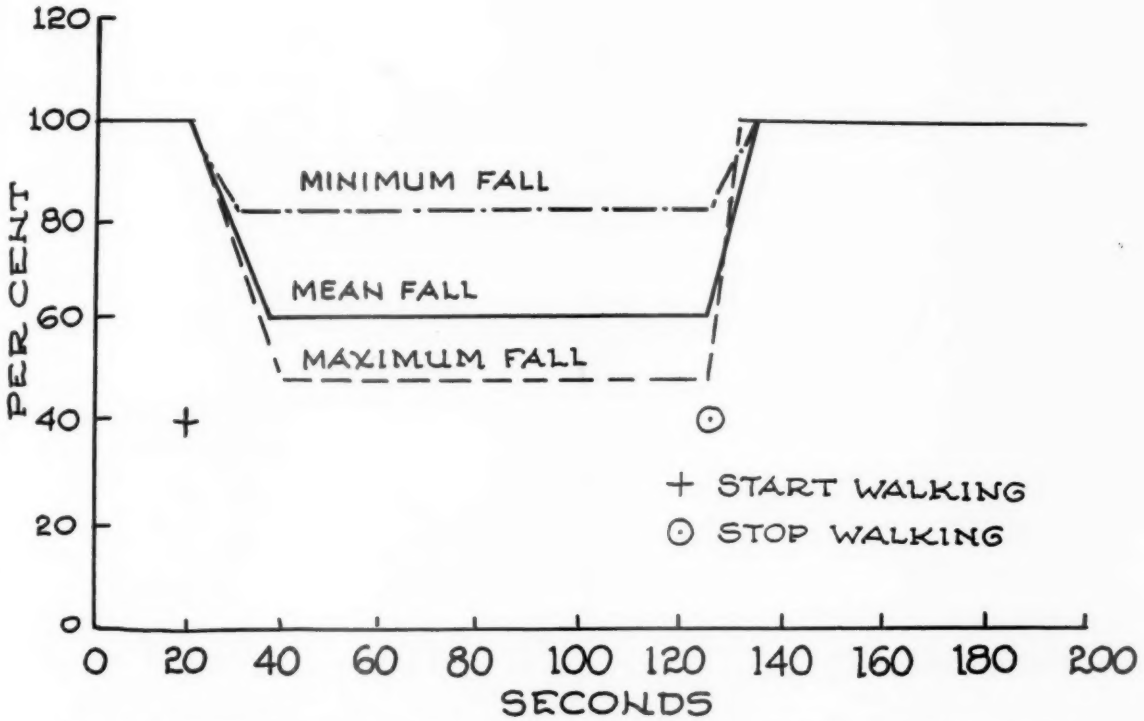

Fig. 3.—Ambulatory venous pressure patterns observed in 12 extremities of 11 patients suffering from the "postphlebitic syndrome."

In Patient L. R., exhibiting a postphlebitic syndrome and proved incompetence of the valves of the deep veins, observations before and after popliteal vein ligation demonstrated (Fig. 4) a sharp rise in the ambulatory venous pressure after the procedure. In Patient E. H., also previously reported, a right superficial femoral vein ligation was done for a similar condition. This was followed by a marked increase in edema and a striking rise in the ambulatory venous pressure. As indicated in Fig. 5, this increase in the ambulatory venous hypertension has persisted and even increased over an 8 month period in spite of no episode of fresh thrombosis. The edema has persisted in spite

of vigorous compressive therapy. The latest pressure studies reveal a high grade of venous obstruction. Unusual observations were made during the latest venous pressure study. Initially on ambulation (Fig. 6) a slow fall of 24 cm. of water (18 per cent) occurred, followed by a secondary rise during ambulation. With the application of a tourniquet to obliterate the superficial veins a pressure fall of only 10 cm. occurred on ambulation, and required 21 seconds to be effected. During this period of repeated ambulation, edema of the leg visibly increased. With further ambulation subsequent to removal of the tourniquet the pressure no longer fell, but rose 6 cm. This demonstrates

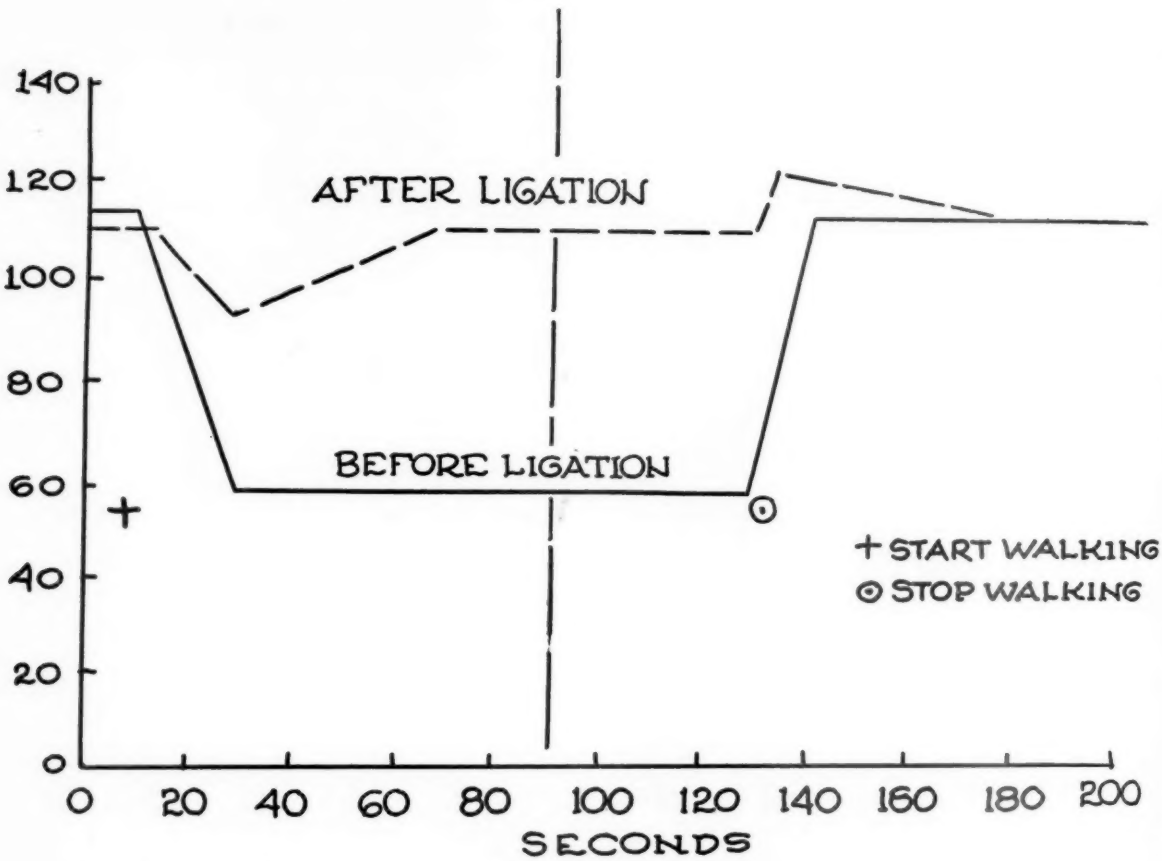

Fig. 4 (Patient L. R.).—Postphlebitic syndrome with ulceration. Ambulatory venous pressure patterns before and 12 days after popliteal vein ligation. There is evidence of an extreme degree of venous obstruction following the operative procedure.

a significant increase in ambulatory venous pressure incident to increasing edema. It should be noted that during these changing venous pressure patterns the cannula at all times appeared open with a free flow of fluid in and out of the vein.

Observations previously reported in 9 additional individuals 6 months to 6 years following ligation of the superficial femoral vein or, in 2 instances, the common femoral vein (Fig. 7) revealed persistent ambulatory venous hypertension in the entire group with no evidence of development of collateral veins served by competent valves. These studies have convinced us that, in spite of

some favorable clinical reports,[1, 7] there is no apparent rational basis for ligating deep veins of the legs in patients exhibiting the postphlebitic syndrome with valvular incompetence.

Clinical observations have indicated that chronic conditions of the lower legs resulting from trauma, cellulitis, lymphangitis, ankylosis, obesity, primary varicose veins, and many other conditions[2, 8, 13, 14] may resemble closely

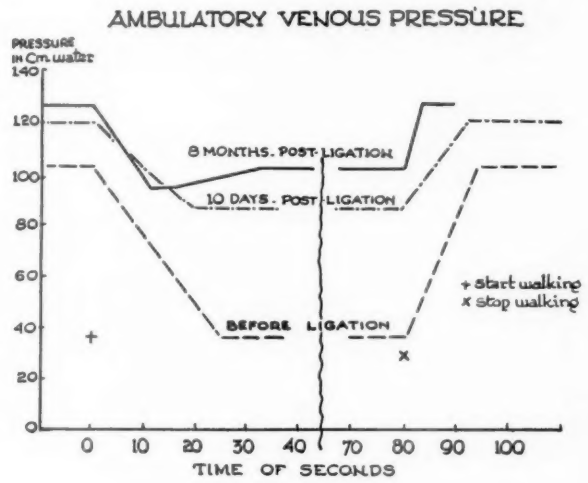

Fig. 5 (Patient E. H.).—Postphlebitic syndrome with bilateral edema of legs. Left superficial femoral vein ligation followed by pronounced increase in edema of left leg. Venous pressure studies before, 10 days, and again 8 months after operation. Marked and progressive increase in venous hypertension is observed following the operation.

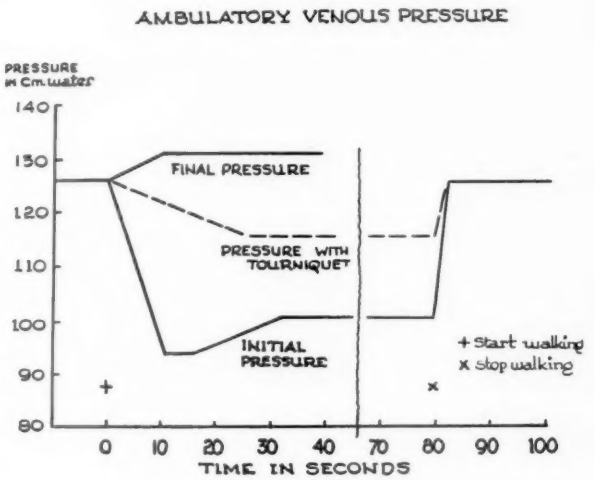

Fig. 6 (Patient E. H.).—Ambulatory venous pressure studies 8 months following superficial femoral vein ligation for postphlebitic edema. A progressive increase in the venous hypertension is apparently due to rapidly increasing edema of the leg. (See Fig. 5.)

the postphlebitic syndrome. The inclusive, noncommital term "lower leg syndrome" has been used for this entire group of conditions. How frequently these conditions are associated with an occult phlebitis, and how frequently this syndrome may occur in the absence of venous disease is not known.

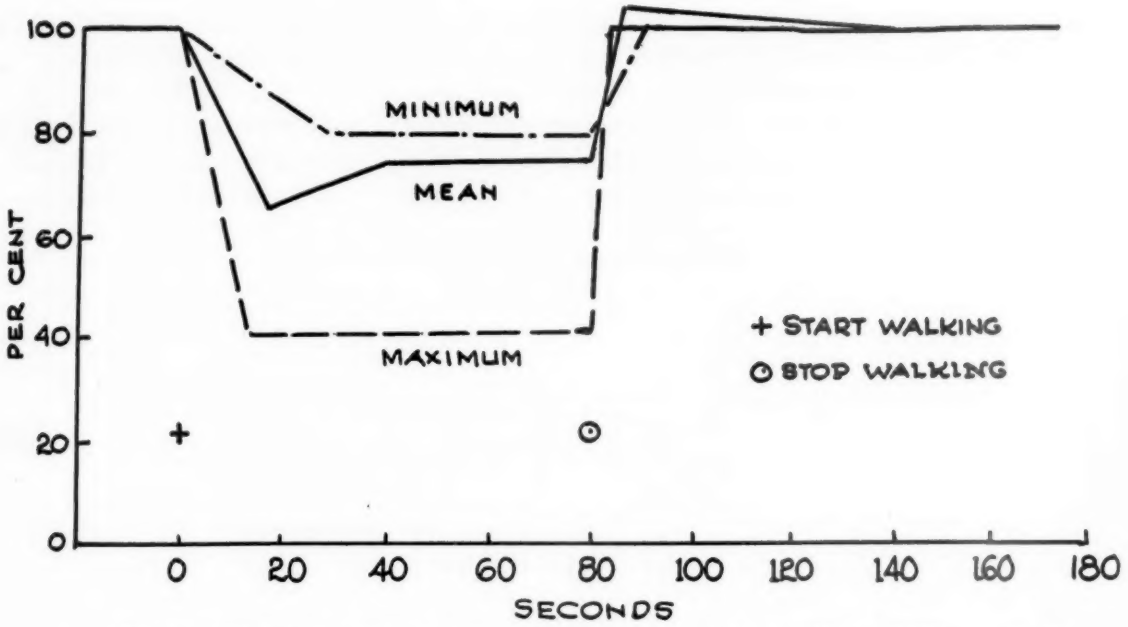

Fig. 7.—Ambulatory venous pressure patterns observed in 9 patients studied 6 months to 6 years following ligation of the deep venous system of the lower extremity. Maximum, minimum, and mean degrees of fall are indicated.

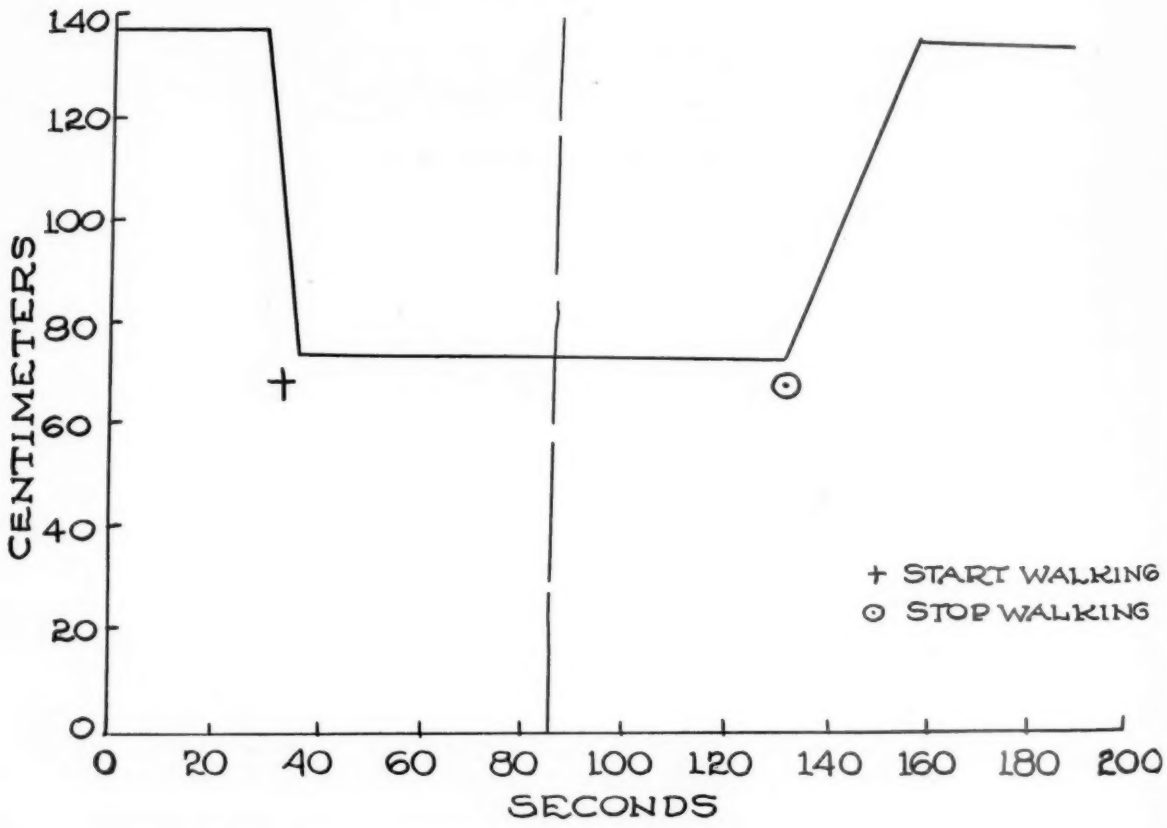

Fig. 8 (Patient S. O.).—Crushing injury of right leg with fracture followed by persistent edema and severe lower leg syndrome with ulceration. Ambulatory venous pressure pattern indicates absence of venous hypertension and presence of competent valves in the veins.

Ambulatory venous pressure studies in Patient S. O., previously reported, suggested that this test might be useful in demonstrating the presence or absence of valvular incompetence and venous congestion in patients exhibiting the lower leg syndrome and in whom the etiology was doubtful. This 57-year-old white man had suffered a severe crushing injury of the right leg with fracture of the tibia 19 years earlier. This was followed by persistent edema, recurrent infection, pigmentation, induration, and finally recurrent indolent ulceration. On examination the patient exhibited severe edema of the leg and thigh with pigmentation and induration of the lower leg surrounding a large ulcer on the anteromedial aspect. We thought, clinically, that this represented a posttraumtic phlebitis with its attendant complications. Ambulatory venous pressure studies (Fig. 8) indicated no venous obstruction and the presence of

Fig. 9 (Patient S. O.).—Retrograde phlebography confirms the presence of competent valves in the deep veins and demonstrates their normal appearance. (See Fig. 8.)

competent valves in the deep venous system. This was confirmed by retrograde phlebography (Fig. 9). In the absence of significant vasoconstriction, this patient undoubtedly represents an example of lymphedema, recurrent cellulitis, and fibrosis in the absence of demonstrable venous disease.

The findings in this case prompted us to make venous pressure studies in other individuals with chronic leg disorders in whom the etiology was not apparent, or in whom phlebitis did not appear to be the primary factor.

POSTTRAUMATIC LOWER LEG SYNDROME

Three individuals were studied in whom the onset of symptoms apparently followed a traumatic episode.

CASE 1.—V. C., a 48-year-old white man, at the age of 23 sustained severe trauma to the anterior aspect of the right lower leg with avulsion of a large amount of tissue. The wound healed slowly, and since that time repeated ulceration of the area occurred incident usually to secondary trauma. The presenting ulcer was said to be 1 month old, but examination revealed an elevated, foul-smelling ulcer 4 cm. in diameter surrounded by an area of pigmentation and moderate edema. There was roentgen evidence of underlying periostitis. Venous pressure determinations (Fig. 10) revealed a satisfactory sustained fall of 71 cm. (50 per cent) in pressure on ambulation and an almost normal slow rate of increase in pressure on cessation of exercise. This indicates an essentially normal venous system. Histologic examination of tissue from the ulceration revealed an epidermoid carcinoma, grade 2. In this instance the severe trauma and subsequent recurrent ulceration was not associated with any significant functional change in the venous system. The presence of normal deep veins and valves was confirmed on subsequent examination of the extremity.

CASE 2.—C. G., a 55-year-old Negro man, sustained a bullet wound of the right ankle 20 years ago. Localized swelling of the ankle persisted. One year ago he kicked the medial aspect of the lower leg and a persistent ulcer developed which measured 2.5 by 4.0 cm. at the time of examination. The leg had the appearance of a mild "lower leg syndrome" with moderate edema and pigmentation surrounding the area of ulceration, and several small pale scarred areas. There was moderate varicosity of the internal saphenous vein in the mid-leg with smaller varices underlying the area of pigmentation. The varicosities did not decrease in size on ambulation with a tourniquet applied to the mid-leg. The recumbent and erect resting venous pressures were within normal limits. On ambulation (Fig. 11) a moderately slow fall of 57 cm. (46 per cent) occurred, with a moderately rapid 14 second rise in pressure on cessation of ambulation. The pattern was unchanged with a tourniquet obliterating the superficial veins. In this instance a moderate degree of valvular incompetence is apparently present.

CASE 3.—P. F., a 48-year-old white woman, gave a history of a fracture of the right ankle 15 years before, with subsequent edema localized to the fracture area. Gradually there appeared a brawny induration and pigmentation of the entire circumference of the lower half of the leg. At the end of a long day on her feet the pigmentation would be more pronounced and slight edema would appear. During the past year a similar but milder process had developed spontaneously in the left leg. Mild varices were present in the right calf and were considerably improved on walking with a tourniquet placed below the knee. She gave no history to suggest a phlebitic episode. However, the appearance of a similar condition spontaneously in the other leg suggested that the trauma may not have been the primary factor in the development of the lower leg syndrome on the right. The recumbent and erect resting venous pressures were normal, whereas on ambulation (Fig. 12), a fall in pressure of only 22 cm. (17 per cent) occurred, with a very rapid rise in pressure on stopping ambulation. Repetition of the test with the superficial veins obliterated by a tourniquet revealed an even greater venous hypertension. Peripheral phlebography revealed marked constriction of long segments of the tibial veins at the knee.

In the absence of history to suggest phlebitis, and in the presence of only a slight amount of edema, these studies nevertheless demonstrate a severe degree of venous congestion. Whether this developed spontaneously, or incident to the ankle fracture, is difficult to determine.

Occasionally a patient gives a history of long-standing edema and repeated trauma leading to the lower leg syndrome. It is often difficult, as in the next reported case, to determine the significance of the several historical factors leading to the development of the syndorome.

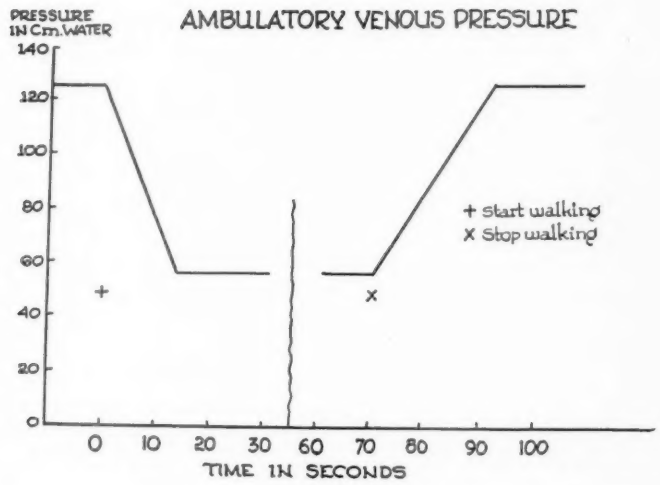

Fig. 10 (Case 1, Patient V. C.).—Recurrent posttraumatic ulcer of leg with malignant degeneration. Ambulatory venous pressures indicate essentially normal venous physiology.

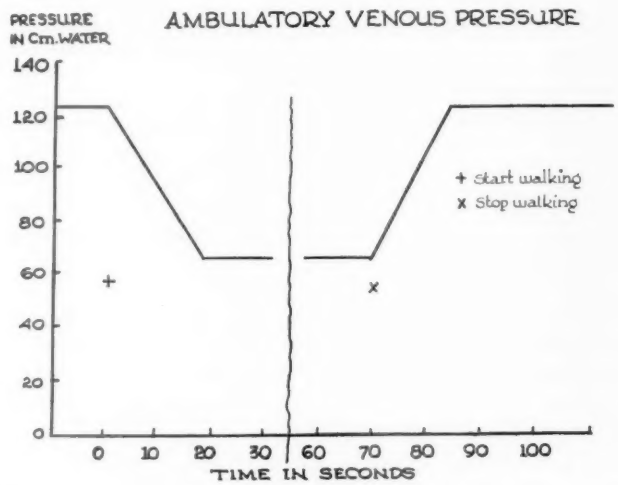

Fig. 11 (Case 2, Patient C. G.).—Posttraumatic edema and ulceration of the leg was present. The venous pressure pattern is moderately abnormal.

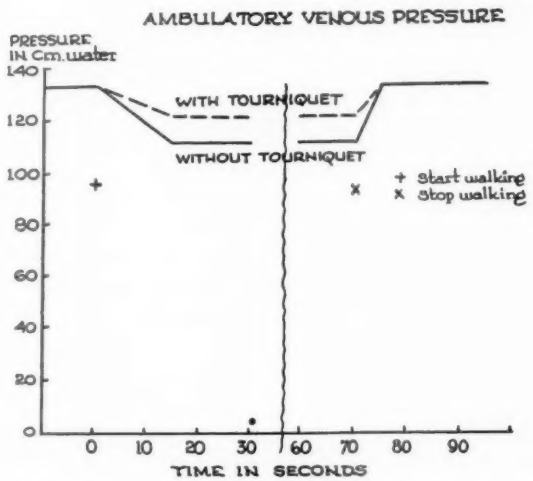

Fig. 12 (Case 3, Patient P. F.).—Slight edema, pigmentation, and brawny induration were present following fracture of the right ankle. Marked ambulatory venous hypertension is present.

CASE 4.—L. R., a 58-year-old Negro woman, gave a 2 year history of spontaneously appearing pigmentation of the anteromedial aspect of the left ankle and lower leg. Seventeen, and again 14, months prior to admission she struck her left leg. Subsequently slight edema and moderate varicosities appeard. An ulcer developed at the site of trauma and persisted to the time of admission to the Vascular Clinic. It healed rapidly on compression therapy. Examination revealed marked pigmentation on the medial aspect of the ankle and the lower leg. Moderate varicosities were present and the tissues in this area were indurated. On cannulating the internal saphenous vein at the ankle it was found to be markedly sclerotic. The recumbent antecubital pressure was 15 cm., the recumbent pedal pressure 19 cm., and the resting erect pressure 5.5 cm., all within normal limits. However, on ambulation (Fig. 13) with or without a tourniquet, a marked degree of venous congestion was evident with an initial fall of 19 cm. (16 per cent), a secondary rise in pressure of 6 cm. during ambulation, and a postexercise rise in pressure 6 cm. above the resting level. Apparently an insidious thrombosis occurred in this patient with ulceration being precipitated by repeated trauma. Peripheral phlebography revealed a severe constriction of the popliteal vein.

It is thus apparent that among these patients in whom trauma appeared to be a major factor in the development of the lower leg syndrome, the functional status of the deep venous system ranged from normal to one of severe congestion.

APPARENTLY SPONTANEOUS EDEMA AND THE LOWER LEG SYNDROME

It is not uncommon for a patient to give a history of apparently spontaneous edema developing insidiously. The question arises whether or not this condition is due to an occult phlebitis. The following cases illustrate this problem.

CASE 5.—N. B., a 10-year-old Negro boy, developed spontaneous swelling of the right leg 1 year earlier, which lasted about 10 days, regressed, and did not recur. Six weeks before examination he developed swelling of the left leg which persisted, though showing some improvement the preceding week. Examination revealed a moderately severe soft edema of the left leg extending to the knee. No other changes were present except for the presence of bilaterally enlarged, soft, nontender inguinal lymph nodes. The recumbent antecubital venous pressure was 12.0 cm., the recumbent pedal pressure 22.0 cm., and the resting erect pressure 2.0 cm. On ambulation (Fig. 14) without a tourniquet there was a moderately rapid fall in pressure of 41 cm. (44 per cent) which was maintained until walking ceased, when a rapid (7 second) rise to the resting level occurred. With the application of a tourniquet to obliterate the superficial veins, or with digital compression of the internal saphenous vein alone, the fall in pressure on ambulation was only 10 cm. (11 per cent), and the pressure rise after exercise was even more rapid (3 seconds). These studies demonstrated a severe degree of deep venous obstruction. The internal saphenous vein was able largely to compensate for the deep venous thrombosis.

CASE 6.—J. M., a 17-year-old girl, experienced the insidious onset of edema of the left leg 1 year ago. No fever, pain, chills, color or temperature changes occurred. The edema was moderately severe at the end of a day spent on her feet, but was almost entirely absent on arising in the morning. Easy fatigability of the leg was present. Considerable improvement occurred following two lumbar sympathetic blocks. Examination revealed moderately severe edema of the left leg extending to the knee. No pigmentation, induration, or inflammation was present. The recumbent antecubital venous pressure was 16 cm., the recumbent pedal pressure 22.5 cm., and the resting erect pressure 1.0 cm. On ambulation (Fig. 15) a rapid fall of 63 cm. (54 per cent) occurred and persisted. On cessation of exercise a rapid (7 second) rise in pressure occurred. The pressure pattern was not altered following obliteration of the superficial veins with a tourniquet.

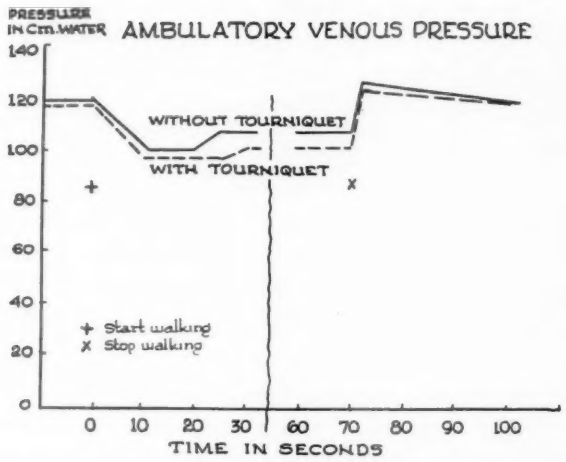

Fig. 13 (Case 4, Patient L. R.).—Spontaneous pigmentation was present for 2 years, followed by moderate varicosities, slight edema, and ulceration. Skin changes were severe and the internal saphenous vein was sclerotic. A marked degree of venous congestion is indicated by the venous pressure studies.

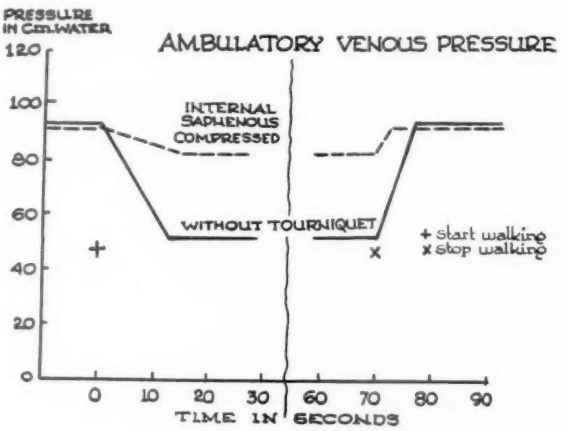

Fig. 14 (Case 5, Patient N. B.).—Spontaneous temporary swelling of right leg appeared 1 year ago. Left leg developed persistent spontaneous edema 6 weeks prior to study of left leg pressures. Moderately severe pitting edema was present. Study indicates patent superficial veins with a severe obstruction of the deep venous system.

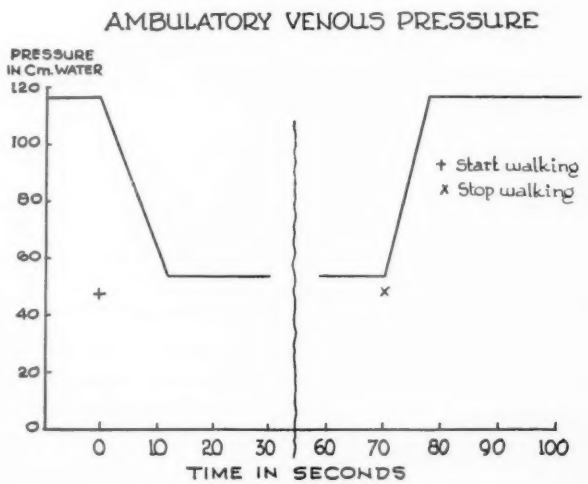

Fig. 15 (Case 6, Patient J. M.).—Insidious onset of persistent soft edema of left leg occurred 1 year before study. No other changes were present. Subjective and objective improvement followed 2 lumbar sympathetic blocks. Ambulatory studies indicate incompetence of the valves but little venous obstruction.

These studies indicate that a considerable degree of valvular incompetence was present without marked venous obstruction. This is in contrast with the severe deep vein obstruction in Patient N. B., who was seen soon after the onset of edema.

CASE 7.—R. B., a 30-year-old Negro woman, apparently had a chronic extensive pretibial ulcer sometime during childhood. This healed without residual edema. At the age of 28, a diagnosis of addisonian anemia was established. Six months prior to study she spontaneously developed edema of the left leg. She complained of mild pain in the thigh but had no fever. At that time severe anemia was present. When the patient was examined in the Vascular Clinic 6 months later extensive pigmentation, edema, induration, and fibrosis were present in the left lower leg, evidencing a lower leg syndrome of considerable severity. The recumbent antecubital and pedal venous pressures were 16.5 and 17.5 cm., respectively. The resting erect pressure was 7.0 cm. On ambulation (Fig. 16) a rapid and moderate primary fall in pressure of 48 cm. (40 per cent) occurred. This was followed by a significant secondary rise of 15 cm. in pressure during continued ambulation, with a postexercise rise to above the resting level, the pressure then slowly returning to the resting level. Ambulation with a tourniquet applied resulted in a somewhat greater initial fall in pressure, 57 cm. (48 per cent), but with a persistence of the secondary rise during ambulation and the postexercise overswing.

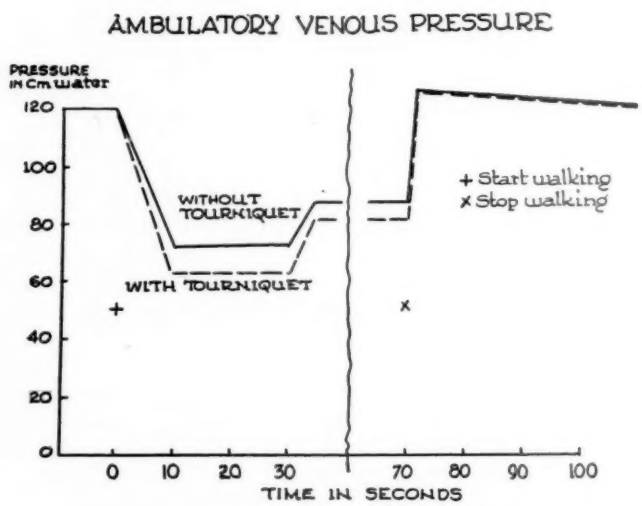

Fig. 16 (Case 7, Patient R. B.).—A pretibial ulcer was present in childhood. Addisonian anemia was known for 2 years. Spontaneous edema of left leg was present for six months. Venous hypertension was severe with continued ambulation.

This illustrates a striking difference in the adequacy of the venous system at rest and on prolonged ambulation. The moderate improvement when the superficial veins were obliterated suggests that reflux down the superficial veins had contributed to some extent to the ambulatory venous hypertension.

"PRIMARY" VARIOSE VEINS AND THE DEEP VENOUS SYSTEM

CASE 8.—N. W., a 59-year-old Negro woman, gave a history of severe varicosities of long standing, more marked on the left side. These first appeared with her first pregnancy and had progressed ever since, being aggravated by numerous subsequent pregnancies. She gave no history suggesting phlebitis or cellulitis. Two years prior to study, after repeated trauma to the medial aspect of the left foot caused by flying pieces of chopped wood, an ulcer appeared over large varices present below the internal malleolus. Six months prior to our

study the patient had a high excision and 2 below-the-knee excisions of very large varicosities. The ulcer healed promptly, although a concomittant dermatitis required 5 months to resolve. On examination the leg was much improved, with disappearance of pigmentation and a soft pliable skin. The patient was delighted with the result, although moderate varicosities were still present in the mid-leg and very large ones were present just above and below the internal malleolus. These varices did not improve during the comparative tourniquet test even with a tourniquet placed low on the leg. On the basis of the history, the response to saphenous ligation, and the physical findings, it seemed likely that the lower leg syndrome in this individual was due to extensive primary varicosities complicated finally by repeated trauma. The recumbent antecubital, recumbent pedal, and resting erect venous pressures were 16.5, 17.0, and 9.0 cm., respectively. On ambulation (Fig. 17) only a minimal fall in pressure of 23 cm. (17 per cent) occurred, but this was not associated with a secondary rise during ambulation or an excessive rise subsequent to exercise, although the post ambulation rate of pressure rise was very rapid. There was no alteration in the pattern following obliteration of the superficial veins by tourniquet.

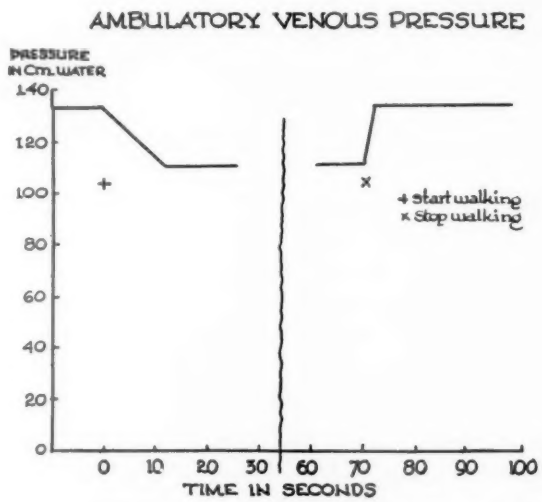

Fig. 17 (Case 8, Patient N. W.).—Severe varicosities of long standing were present with pigmentation and finally ulceration following trauma. High and 2 low internal saphenous vein excisions resulted in healing of ulcer and resolution of the pigmentation, but large varicosities were still present around the ankle. These did not empty on ambulation with a tourniquet about the lower leg. Incompetence of the deep vein valves and ambulatory venous hypertension are present.

These studies demonstrate incompetence of the valves in the deep venous system. Obstruction may be a factor but the pattern suggests primarily an excessive reflux flow of blood down the valveless deep veins. The absence of severe obstruction correlates well with the striking clinical improvement which followed the saphenous vein surgery. It is to be noted that the failure of the varicosities to empty on ambulation even with a tourniquet placed at a low level was associated not only with incompetence of the valves of the communicating veins but also a demonstrated incompetence of the valves of the deep veins. Such findings with the comparative tourniquet test indicate either valvular incompetence of the deep system or deep vein obstruction. If the deep veins are not obstructed, and their valves are competent, blood entering from the capillary bed will, during ambulation, rise rapidly in the deep veins because of the low pressure present. There will be little or no tendency for

such blood to flow into superficial veins at the same level even though the valves in the communicating veins are incompetent, because the pressure in the superficial veins will tend to be higher than in the deep system. Reflux filling of the superficial veins will have to occur through the upper reaches of the superficial venous system. We feel, as do others,[9] that persistence of filling of varicosities during the comparative tourniquet test, or the occurrence of a prompt "double positive" Trendelenburg test, indicates incompetence of the valves in the deep venous trunks as well as those in the perforating veins.

DIFFERENTIATION OF CELLULITIS AND PHLEBITIS

In some instances it is difficult to determine from the history and the physical findings whether a lower leg syndrome is the result of repeated cellulitis alone, or cellulitis complicating an occult phlebitis. The following study illustrates the assistance which may be obtained from ambulatory venous pressure determinations.

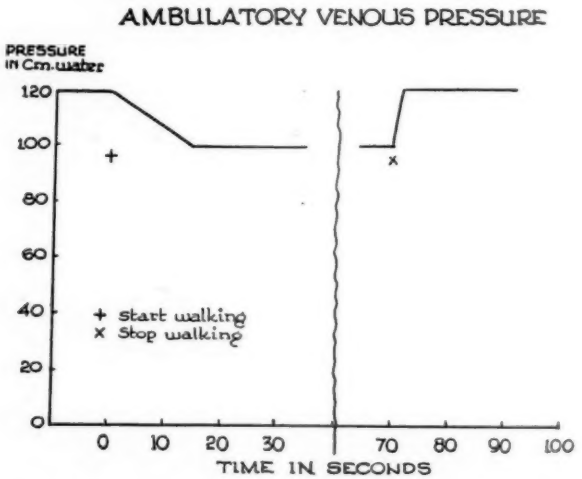

Fig. 18 (Case 9, Patient V. L.).—There is a history suggesting cellulitis rather than phlebitis 12 years ago, followed by localized pigmentation and recurrent ulceration. Scarring, pigmentation, and induration were present. Marked ambulatory venous hypertension is present.

CASE 9.—V. L., a 43-year-old Negro woman, gave a history of a painful, red, hot, swelling in the left leg 12 years before. The area involved was apparently limited to the medial aspect of the lower half of the leg. Several months later small blisters formed in the area and finally ulcers appeared. These have healed and recurred several times. In 1940 the patient had a ligation of the internal saphenous vein below the knee. An ulcer was present on examination and had been present for the past year. This was associated with scarring, induration, and pigmentation of the medial aspect of the left lower leg. The history and physical findings suggested that the lesion might be primarily the result of a severe cellulitis. The recumbent antecubital and pedal venous pressures were 15 and 11 cm., respectively. On standing quietly erect the pressure just equalled the level of the heart. On ambulation (Fig. 18) a marked venous hypertension was present as evidenced by a 20 cm. (17 per cent) fall in pressure with or without tourniquet compression of the superficial veins. A rapid rise in pressure occurred on stopping the exercise.

It is apparent that serious changes had occurred in the functional status of the veins. Peripheral phlebography revealed extensive constriction of the femoral vein in the upper thigh.

DISCUSSION

Measurement of the peripheral venous pressure in extremities during activity as well as at rest is proving to be an increasingly valuable means of study of circulatory physiology. Recently additional studies have been reported by Højensgård and Stürup.[6] They have contrasted the findings in a series of patients with "primary" varicose veins with those in patients in whom varicosities had appeared subsequent to a deep thrombophlebitis. They used Hansen's[4, 5] recording manometer with an intravenous cannula and reported no fall in pressure on ambulation in a majority of postphlebitic patients either with or without tourniquet obliteration of the superficial veins. In a small group the pressure did fall on ambulation when the superficial veins were compressed. In patients with "primary" varicose veins the pressure fell on ambulation if the valves were competent, or if incompetent superficial veins were compressed. They also demonstrated the transmission of high intra-abdominal pressure waves down veins having incompetent valves.

The changes in venous pressure which we have observed in postphlebitic patients on ambulation have occurred over a much wider range than these reported by the Danish workers,[6] as well as the series reported by White and Warren.[12] The report of Pollack and associates[10] shows more variation than the other series but still not as great as ours. We have found some degree of pressure fall on ambulation in a higher percentage of the postphlebitic patients. It is difficult to know whether this is due to a difference in case selection, to somewhat more vigorous exercise (lifting both feet 15 cm. 60 times a minute), or to a difference in the size of the intravenous cannula and the type of manometer used.

The technique we employ is a simple one which can be used as a clinical diagnostic tool as well as a method of clinical investigation. As demonstrated in this study it may be used either alone or in combination with phlebography to clarify the etiology of certain chronic leg conditions. Accurate quantitation of venous congestion may be achieved. It also provides a means of checking and developing the accuracy and significance of the classical tests of Trendelenburg, Perthes, Mahorner-Ochsner, and others.

CONCLUSIONS

In a patient with a postphlebitic syndrome and valvular incompetence of the deep veins for whom a superficial femoral vein ligation was performed, a marked increase in the ambulatory venous hypertension occurred postoperatively and has persisted and progressed over an 8 month period. Increasing ambulatory venous hypertension was found to accompany increasing edema.

Ambulatory venous pressure studies have assisted in determining the presence of disease of the deep veins in a series of patients exhibiting chronic dis-

orders of the lower leg associated with trauma, spontaneous edema, cellulitis, and "primary" varicose veins. It has been demonstrated that in some post-traumatic conditions associated with edema, pigmentation, fibrosis, and ulceration the venous system is apparently entirely normal. In other individuals in whom no definite historical evidence of phlebitis is present in association with trauma, infection, or varicosities, these studies have revealed serious degrees of ambulatory venous hypertension. In some instances this was unquestionably due to venous obstruction, in other instances it was due either to venous obstruction, to venous valvular incompetence, or to a combination of the two.

Functional changes may be compared with anatomic changes by correlation with appropriate phlebography.

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THE DEEP VEIN VALVES

A Venographic Study in Normal and Postphlebitic States

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IT IS well known that the veins of the extremities are equipped with valves whose function it is to aid in the upward flow of blood, particularly when the body is in the erect position. These valves are also supposed to prevent reflux down the veins of the extremities when sudden increase in pressure occurs from muscular action in the thoracic and abdominal cavities. In the leg, the common femoral, superficial femoral, and deep femoral veins and their tributaries are well equipped with these valves and it has hitherto been assumed that this mechanism is an efficient one. A parallel has been drawn with the great saphenous vein, where retrograde injection attempted in a normal vein is impossible no matter what pressure is used, whereas such an injection in a true varicose vein with incompetent valves is accomplished with ease. Until now, the normal deep vein valve stations have been considered as efficient as those in the saphenous system.

Recently, considerable attention has been paid to deep venous valvular incompetence subsequent to a previous deep thrombophlebitis as being the main reason for the common postphlebitic complications of ulcer, eczema, and indurations. Operations have been devised which interrupt the incompetent deep veins either in the upper femoral or popliteal regions and so supposedly prevent the retrograde transmission of increased intra-abdominal venous pressures. These operations are based on studies of venous pressure in these affected limbs showing marked increases during straining and slight increases when in the upright position. The therapeutic conclusions have all been based on cases of postphlebitic vein damage with little comparison to the normal individual.

It is the purpose of this presentation to present the findings in 52 cases where retrograde venography was carried out in established cases of previous deep thrombophlebitis and in cases where the deep venous system was supposedly normal. Two techniques have been followed:

Technique 1.—With the patient lying on the x-ray table, and using local anesthesia, a direct venipuncture is made into the common femoral vein. An assistant compresses the femoral vessels against the pubic ramus, closing the vein centrally. The injection of Diodrast (20 c.c.) is made without undue pressure and films are taken of the thigh and leg.[2] Criticism can be leveled at this method as being unphysiologic and not demonstrating the true vein and valve picture because of the production of abnormal venous pressures. Consequently, technique 2 was adopted.

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Technique 2.—During the course of high saphenous ligation for varicose veins or in postphlebitic legs where a retrograde venogram is desired,[4] a small Coudé catheter is introduced through the saphenous stump with its tip directed distally into the common femoral vein. The patient is transported to the x-ray room and placed upright on the tilt table. Diodrast injection is carried out through the catheter and 3 pictures are taken in rapid succession with the patient taking a deep breath and straining before each picture.

Fig. 1.—Retrograde venogram of patient complaining of some enlargement of leg and dependent cyanosis. No history of phlebitis or varicose veins. Congenital absence of valves in femoral vein is present, allowing complete retrograde flow.

RESULTS IN SUPPOSEDLY NORMAL VEINS

Group I.—Three patients were investigated for slight chronic leg enlargement with increased cyanosis and dilated cutaneous venules. They had the complaints of aching and a feeling of heaviness and tiredness of the leg when upright for prolonged periods. No edema was present and the symptoms were worse at the time of the menses. Retrograde venography (Fig. 1) gave an identical picture of a valveless common and superficial femoral vein extending, in 2 cases, into the anterior and posterior tibial branches. The femoral tributaries showed valves, but decreased in number. It is my feeling that this is a definite entity; it was described by me in 1941.[1] The leg enlargement is probably due to a congenital absence of valves in the deep veins resulting in venous retardation on straining or when upright. It is interesting to note that no cutaneous malnutrition changes were present in the leg in any of the 3, even though all of them

were over 20 years of age. One can argue, therefore, with some justification, that the changes in the postphlebitic leg are not solely due to venous incompetence and increased venous pressures.

Group II.—Twelve individuals had retrograde venograms performed by the catheter technique during the course of high ligation of the great saphenous vein for varicose veins. All these cases were uncomplicated, without evidence of edema or other leg abnormalities, and, consequently, one presumed that the deep veins were normal. Four normal legs were investigated by the first technique. In 3 instances, with a catheter in the deep vein, no vein shadow was seen. No explanation can be offered except that possibly the patient failed to force down at the time of x-ray. The remainder (Figs. 2, 3, and 4) showed varying degrees of retrograde filling of the vein, the solution easily passing through normal valve stations and being stopped by others.

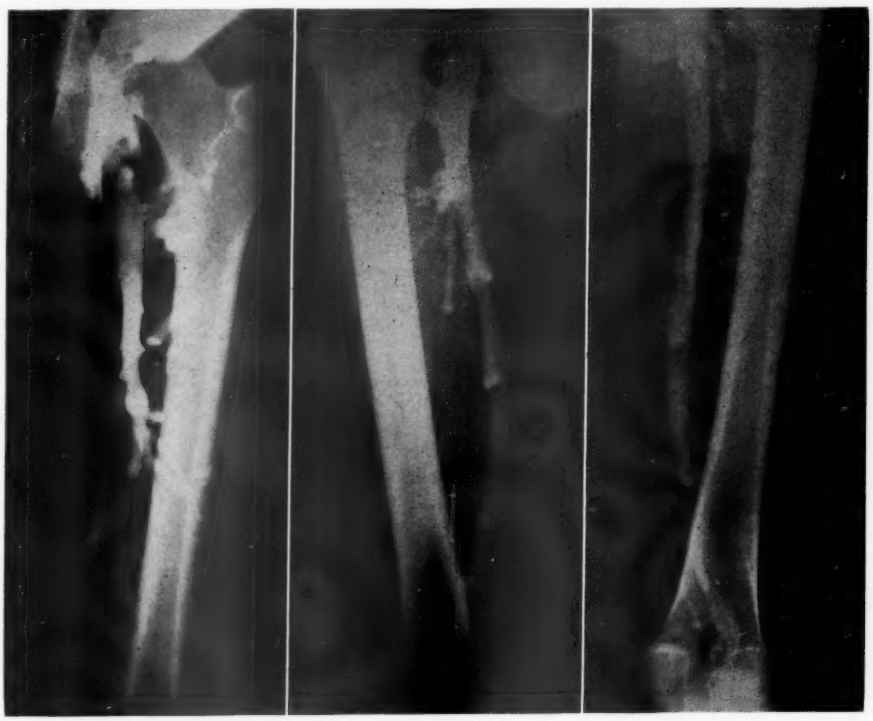

Fig. 2. Fig. 3. Fig. 4.

Figs. 2, 3, and 4.—Retrograde venograms done at the time of high saphenous ligation for varicose veins. No symptoms or signs were present to indicate deep venous incompetence and yet retrograde flow was permitted in varying degrees because of valvular incompetence.

The interpretation placed on these findings, especially when done by the catheter technique, is that supposedly normal vein valves may vary greatly in their function, allowing blood to flow in a retrograde direction in many cases when the intra-abdominal pressure is raised. The assumption therefore, is that the deep valvular system is not perfect in function and cannot be compared with locks in a canal. It is likely that valvular efficiency varies from person to person and that some retrograde flow should be considered a normal

phenomenon. It is possible that the greater degrees of this incompetence account for the aching legs of some women at the time of the menses or of those who have been on their feet for prolonged periods. The symptoms are similar to varicose veins, but occur in their absence.

RESULTS IN DISEASED VEINS

Thirty-two individuals who had a definite history of a previous deep thrombophlebitis and who presented themselves with the typical postphlebitic complications were studied by retrograde venography. Twenty-eight were studied by the direct puncture method and 4 by the catheter technique. Satisfactory pictures were obtained in 18 of the 28 and in all of the cases done by the catheter technique.

Fig. 5. Fig. 6. Fig. 7.

Figs. 5, 6, and 7.—Retrograde venograms in patients with a previous deep thrombophlebitis. The typical findings include valvular incompetence, deformity of the lumen of the main vein, dilatation of collaterals, and incompetence of the great saphenous vein.

In an attempt to find out why, in the 10 failures, the femoral vein could not be found by venipuncture, 4 of these patients were admitted for exploration of the common femoral vein. In each instance this vein was found to be a firm white cord with a thickened wall with marked periphlebitic fibrosis. Biopsy of this vein revealed organized thrombus formation with small areas of recanalization. Nature had produced an almost complete pathologic vein ligation, but the postphlebitic complications were just as severe in these patients as in those who showed a still patent deep vein.

In those individuals in whom a successful venogram was obtained, the results were not unexpected and revealed valvular incompetence with varying degrees of deep vein deformity (Fig. 5), collateral dilatation (Fig. 6), and saphenous varices (Fig. 7). One case done recently showed a remarkable picture (Fig. 8) inasmuch as the catheter, when inserted through the saphenofemoral junction, went into a large, unsuspected, accessory saphenous. The resultant picture showed deformity and retrograde flow in this accessory saphenous, but also, by good fortune, the x-ray plate included the opposite leg and revealed a retrograde venogram on this leg also. The opposite leg had not been involved by phlebitis and was symptomless. This leg was supposedly normal and yet a retrograde filling occurred. The Diodrast must have mounted to the vena cava on the diseased side and been forced down the good leg when the patient strained. This case is an added example indicating the relative incompetence of supposedly normal valves and we plan, in the future, to include both legs in the x-ray film.

Fig. 8.—Retrograde venogram done by the catheter technique through the saphenofemoral junction demonstrating an unsuspected accessory saphenous vein. The Diodrast has also mounted to the vena cava and made a retrograde descent into the normal femoral vein of the opposite leg.

DISCUSSION AND CONCLUSIONS

These investigations appear to indicate that competency of the deep vein valves varies tremendously from person to person and that, physiologically, these valves are not the watertight system previously supposed. As in saphenous valves, they can be congenitally weak or absent, but the important point is that such an absence does not lead to the malnutrition changes seen in the valvular incompetence and vein damage of the postphlebitic leg. It would also appear that, in the leg damaged by a deep phlebitis, the degree of deep vein

incompetence has little bearing on the extent, degree, and type of the postphlebitic complications because such complications can occur in the case where almost complete occlusion of the vein has occurred from organized thrombus.

Therefore, I see little rationale in the present vogue of deep vein ligation in these cases at any level. The complications can be healed by the scrupulous avoidance of edema, be it by bed rest with leg elevation or suitable bandaging. In some cases acceleration of healing and a reduced likelihood of recurrence can be accomplished by the recognized procedures of correction of associated incompetent secondary varicose veins, lumbar sympathectomy, and skin grafting.[3] However, the original etiological damage still remains and the continued well-being of the leg will depend upon the care given it by the individual. Edema and trauma must be prevented, and, if the common sense instructions which I have labelled "The New Way of Life" are followed, recurrence of complications is extremely rare. These are instructions given to all postphlebitic patients in an endeavor to reduce venous stasis and lymphedema. I believe this routine to be the most important factor in keeping such a leg free of complications.

The New Way of Life
Instruction for the Continual Care of the Leg Damaged by Phlebitis

1. Wear your elastic stocking from the time you get out of bed until you retire, with the exception of bath time. The stocking should be renewed every 3 months, and it is best to have 2 stockings that can be alternated for cleaning purposes.

2. Do not stand for more than 30 minutes without sitting down for 15 minutes and elevating the leg on another chair. When standing, get into the habit of flexing the toes in your shoes and frequently rising on tip toes.

3. Plan your day so that you can lie down for 2 to 3 half-hour periods and elevate your leg to a 45 degree angle. The back of a small straight-backed chair is useful for this purpose.

4. Whenever you sit down, elevate your leg on a footstool, chair, or chesterfield.

5. At night, raise the foot of the bed on blocks about 6 inches.

6. Apply a bland cold cream to the affected skin at nights about every second day.

7. Avoid irritation to the involved leg, especially in respect to sunburn and hot water bottles.

8. Be extremely careful to prevent bumping or scratching the affected leg.

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RAYNAUD'S DISEASE

A Study of Criteria for Prognosis

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THERE is an extensive literature, dating back to the original report by Maurice Raynaud (1862),[1] on the phenomenon of intermittent spasm of the digital arteries with subsequent acral pallor and cyanosis on exposure to cold. This literature is replete with reports of a descriptive nature, such as the classical article by A. W. Allen,[2] studies related to the etiology of the phenomenon (Lewis;[3] Morton and Scott;[4] Pearse;[5] Spurling and associates;[6] Villaret and associates;[7] Peet and Kahn,[8] and others), and appraisals of the results of dorsal sympathectomy (Adson and Brown,[9] Telford,[10] and Smithwick[11]). Prior to 1936 the understanding of these symptoms was so vague that Hunt[12] was able to collect only 30 cases of true Raynaud's disease from 500 cases reported in the English and American literature. In 1932 Allen and Brown[13] summarized the criteria for differentiating between true idiopathic Raynaud's disease and the Raynaud's phenomenon due to other underlying diseases. However, no study has been published dealing with the course of either the primary or secondary forms of this disorder. Every afflicted patient desires information relative to prognosis and our interest in this matter has been repeatedly stimulated by such requests. In order to answer more confidently and to put our knowledge of the course of Raynaud's disease on a more rational basis, we have studied a large number of cases with these points in mind. This report is concerned with factors relating to prognosis only in true Raynaud's disease as defined herein.

Raynaud's disease is the primary and idiopathic form of the phenomenon of paroxysmal spasm of the digital arteries producing acral ischemia and cyanosis of the digits, bilaterally and symmetrically, in response to cold and emotions; it is usually relieved by warmth. In its severe form there is a recurring, painful spasm, narrowing the local vessels, deforming the digits (usually the fingers), and leading to local ulceration and necrosis. The disease is frequently seen in young women who show other evidence of vasomotor instability.

Raynaud's syndrome is due to paroxysmal spasm of the digital arteries producing acral ischemia and cyanosis of the digits, usually in response to cold, and always as the result of some underlying vascular or other disease. Most common of the underlying diseases are the obliterative vascular diseases (arteriosclerosis obliterans and thromboangiitis obliterans), the collagen diseases (scleroderma, rheumatoid arthritis, dermatomyositis), thermal injury (frostbite and burns), mechanical trauma (use of vibrating tools such as the pneumatic hammer), and the Naffziger syndrome (cervical rib and scalenus anticus syndrome). Raynaud's syndrome may also result from lesions of the central nervous system.

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The use of the preceding definitions obviates the rather meaningless term "Raynaud's phenomenon," which requires qualification, and which serves, in our opinion, more to confuse than to enlighten. In the study to be reported only patients having Raynaud's disease were included. In the 15 year period subsequent to July 1, 1934, over 350 patients were given a diagnosis of Raynaud's disease or questionable Raynaud's syndrome at the University of Michigan Hospital. In order to confirm the diagnosis of Raynaud's disease and to secure an adequate follow-up period only those cases studied between July, 1934, and July, 1946 (a 12 year period), were included in this investigation. Thus information covering a minimum of 4 years has been obtained in all cases and, as a matter of fact, no case has been included in whom the disease has not existed 5 years or more. Allen and Brown have stressed that at least 2 years must elapse in a patient with Raynaud's symptoms to allow one to rule out underlying disorders prior to making a diagnosis of primary Raynaud's disease.

SELECTION OF CASES FOR STUDY AND METHOD OF STUDY

Of the 238 patients with Raynaud's symptoms seen during the 12 year period (1934 to 1946), 119 were shown on follow-up study to meet all the criteria discussed in our definition of Raynaud's disease. The course of the Raynaud's disease in 100 of these patients is known for a minimum of 5 years, and in a few cases, for as long as 50 years or over. Patients in whom arteriosclerosis obliterans (30), thromboangiitis obliterans (24), scleroderma (29), rheumatoid arthritis (16), and other underlying causes for Raynaud's symptoms were present were eliminated from the group to be discussed, as were patients with very mild, early, or completely atypical symptoms.

Follow-up letters were sent to each patient and to the patient's referring physician. In most cases the patient returned to the vascular clinic for evaluation or was still under our care. In 94 cases follow-up information was obtained by correspondence with the patient, the patient's family, or the patient's physician, in 6 cases by re-examination alone, and by both methods in 70 cases. Some patients have been studied elaborately, employing the plethysmograph, to obtain information concerning changes in blood flow in the digits in response to various drugs and stimuli. Patients who had undergone dorsal sympathectomy were studied using sweating tests to determine the extent of denervation. All patients demonstrated true Raynaud's symptoms and signs upon immersion of the fingers in cold water.

No patient whose Raynaud's symptoms were first noted after the age of 49 years has been included. Only 5 patients were 45 years of age or older when their Raynaud's disease had its onset. We have seen some patients with fairly characteristic Raynaud's symptoms beginning after the age of 50 years in whom all pulses in the upper and lower extremities were normally palpable. These patients have not been included in this report because of the grave suspicion, in spite of good pulses, that some degree of arteriosclerosis could be present. As a matter of fact, in such cases the symptoms were rarely severe and follow-up studies have shown them to be nonprogressive.

All cases of bilateral gangrene of the hands (except for the superficial gangrene of the finger tips seen in Raynaud's disease) were eliminated from the

study and, as mentioned, all mild cases not having fairly characteristic color changes in the fingers intermittently and bilaterally on exposure to cold, with numbness and some degree of burning pain, were also eliminated. Accurate information was available concerning the peripheral pulses and only patients are included in whom these were normal.

Undoubtedly some of the cases eliminated from the study were examples of true Raynaud's disease but we felt that if an error were to be made in the necessarily arbitrary selection of cases for study, it would be less serious and add less to existing confusion if criteria were more, rather than less, rigid than necessary. These factors in selection should be kept in mind in interpreting the data obtained in this study and the conclusions based upon it.

RESULTS OF STUDY

In 100 patients with classical Raynaud's disease, selected on the basis of the criteria described, in whom careful study over a period of at least 5 years confirmed the diagnosis, information was obtained relative to the course of symptoms and ultimate prognosis. Sixty patients (60 per cent) noted the onset of the disease between the ages of 11 and 30 years, and 81 (81 per cent) between the ages of 11 and 40 years. Table I lists the age of onset for all cases in the series.

TABLE I. AGE AT ONSET OF RAYNAUD'S DISEASE

AGE (YEARS)	NUMBER OF PATIENTS	
Childhood (to 10)	6	
11-20	26	60 %
21-30	34	
31-40	21	
41-45	11	
46-49	2	
Total	100	

There were 77 females (77 per cent) in the total series and 23 males (23 per cent). These figures correspond closely with those given by Hines and Christenson[14] (79 per cent females and 21 per cent males at the Mayo Clinic).

The duration of the disease from the onset of symptoms until the last follow-up information is illustrated in Table II. It will be noted that all cases included were followed for a minimum of 5 years. Follow-up information in 83 cases (83 per cent) covers from 11 to 55 years. Thirteen patients (of whom 4 had undergone dorsal sympathectomy) are now dead of causes unrelated to Raynaud's disease. In all cases death occurred many years after the onset of

TABLE II. DURATION OF SYMPTOMS AND TOTAL FOLLOW-UP STUDY

AGE (YEARS)	NUMBER OF PATIENTS	
5-10	17	
11-15	23	
16-20	22	
21-30	18	60 %
31-40	14	
41-50	4	
51-55	2	
Total	100	

the disease. Most common causes were carcinoma, apoplexy, and myocardial infarction. Two patients developed acute lupus erythematosus and died respectively 30 years and 40 years after the onset of Raynaud's disease.

Table III shows the course of the disease in the 100 cases in the study. In 69 (69 per cent) of classical cases the symptoms remain more or less stationary. In 12 (12 per cent) the symptoms regressed over a period of years or disappeared altogether (never before the passage of 5 years). In these patients classed as more or less stationary the symptoms were often relieved in the summer months or when residing in warm climates during the winter months. The symptoms would be re-exacerbated by exposure to cold, especially during the winter months or when working in cold water during the summer. Relief could be obtained from an attack by immersion of the hands in warm water. Attacks could be made less frequent and less severe by careful attention to keeping the hands warm and, in many cases, by the avoidance of emotional crises. In perhaps 15 to 20 per cent of cases some degree of improvement was obtained by the administration of thyroid extract and correction of secondary anemia, if present. There are patients in whom attacks can be precipitated by smoking. While in many others there is no obvious correlation between the use of tobacco and the severity of attacks, we have made it a practice to recommend cessation of smoking in all patients with Raynaud's disease. Some of the patients in this series have been benefited by the ingestion of Priscoline while others have not. All of the 69 cases classed as essentially stationary obtained some measure of relief by adherence to the preceding principles of therapy.

TABLE III. COURSE OF RAYNAUD'S DISEASE

EXTENT OF DISEASE	NUMBER OF PATIENTS	
Regression	12	69 %
Stationary	40	
Slight progression	17	
Moderate progression	6	
Severe progression	25	
Total	100	

Six patients (6 per cent) experienced definite progression of their symptoms to a point short of ulceration and necrosis of the finger tips, and to a point at which, in spite of increased frequency of attack and increased pain and disability, they would not yet submit to dorsal sympathectomy.

One-quarter (25 per cent) of the patients in this series progressed to a point at which necrosis, ulceration, and gangrene of the finger tips (in 11 cases, 11 per cent of the total series), or pain and disability required dorsal sympathectomy.

Further analysis of this latter group, which may be termed the severely progressive group, gives some information which would appear to be of value in

TABLE IV. CHARACTERISTICS OF CASES PROGRESSING TO TISSUE LOSS OR SYMPATHECTOMY

SEX	NUMBER	AVERAGE AGE (YEARS)	PER CENT OF PROGRESSIVE CASES
Female	19	23.3	76
Male	6	29.2	24

prognosis. Table IV reveals that the ratio of males to females in the severely progressive group as compared to the series as a whole is about the same. One can say, therefore, that males and females with Raynaud's disease are equally likely or unlikely to progress to such an incapacitating state. Further, it is apparent on reference to Table V, that, at least in our experience, cases of Raynaud's disease beginning in childhood (as is true also of the so-called "hereditary cold fingers") or after 40 years of age are not likely to be progressive. The great majority of progressive cases have their onset between the ages of 15 and 35 years. Severely progressive cases having their onset after the age of 30 years are in the minority (32 per cent of progressive cases and 8 per cent of all cases).

TABLE V. CHARACTERISTICS OF CASES PROGRESSING TO TISSUE LOSS OR SYMPATHECTOMY

AGE AT ONSET (YEARS)	NUMBER OF PATIENTS	
Childhood (to 10)	0	
11-20	9	68 %
21-30	8	
31-40	7	
Over 40 (45)	1	
Total	25	

Finally, as is shown in Table VI, the majority of severely progressive cases will progress to a severe state in from 1 to 7 years. It seems remarkable that a higher percentage of cases does not progress to this state within 2 years. Cases progressing to an advanced degree after 7 years are almost always characterized by other manifestations of marked vasomotor instability (blushing, palpitation, hyperhidrosis, hypertension, acrocyanosis, fainting spells, and so on).

TABLE VI. CHARACTERISTICS OF CASES PROGRESSING TO TISSUE LOSS OR SYMPATHECTOMY

RATE OF PROGRESSION (DURATION IN YEARS)	NUMBER OF CASES
1-4	10 (4 with ulceration or necrosis)
5-7	6 (3 with ulceration)
8-10	1
11-15	6 (4 with ulceration)
16	2
Total	25

PROGNOSIS FOLLOWING SYMPATHECTOMY

In the 12 year period from which cases were selected for inclusion in this study, 40 patients underwent dorsal sympathectomy for Raynaud's disease or Raynaud's syndrome. In 24 of these patients the diagnosis of primary Raynaud's disease has been confirmed by follow-up study. Of the 16 patients having Raynaud's syndrome, 12 had scleroderma, 2 followed frostbite, 1 was associated with definite exposure to heavy metals, and 1 had had an injury to the shoulder with a broken clavicle and thrombophlebitis of the right arm. In no patient having Raynaud's syndrome as a result of arteriosclerosis obliterans[15] or thromboangiitis obliterans[16] was dorsal sympathectomy necessary. Eight patients have also had either unilateral or bilateral lumbar sympathectomy in

addition to dorsal sympathectomy; 4 of these 8 patients had primary Raynaud's disease. Lasting relief of Raynaud's symptoms in the lower extremities was obtained in these 8 cases.

Of the 24 patients with Raynaud's disease, some of whom are not included because of inadequate follow-up information in the 100 cases of Raynaud's disease selected for this study, 20 had marked relief of their Raynaud's disease following dorsal sympathectomy for at least 2 years. In 6 of these recurrence was noted in from 2 to 13 years postoperatively. Ten of the remaining 14 patients, who have had relief for from 4 to 15 years, were available recently for tests for sudomotor activity. One-half of them showed some degree of sweating of the palms during these tests. Angiospastic phenomena were demonstrated in 3 patients who had no sudomotor activity. There was an interesting correlation between the type of dorsal sympathectomy performed and these results. The preganglionic type of operation isolating the second and third dorsal vertebrae after section of the sympathetic trunk below the third dorsal vertebra as described by Smithwick and Telford was performed in 10 of the 40 patients. Postganglionic dorsal sympathectomy with excision of the second and third dorsal vertebrae and sometimes the stellate ganglia was carried out in the remaining 30 patients.

In general, recurrences were noted earlier in the patients having the preganglionic type of operation, and indeed, in a few of these relief was not even obtained immediately after operation. The 5 patients with Raynaud's disease who showed no sudomotor activity on recent study (and of whom 3 had residual although ameliorated angiospastic activity) had all had postganglionic sympathectomies. Two had had excision of the stellate ganglia as well.

These results are in accord with the interesting observations of Felder, Simeone, Linton, and Welch,[17] who noted clinical recurrence in 64 per cent of 40 patients studied carefully 6 months to 20 years after dorsal sympathectomy for Raynaud's disease and Raynaud's syndrome. They concluded that while sensitization (to Adrenalin) may occur in man following postganglionic denervation, it did not play an important role in the patients studied. Instead, recurrences were associated with demonstrably active vasomotor nerve fibers (regenerated preganglionic axones). We agree with them that the ideal operation is one which will completely denervate the extremity and at the same time prevent regeneration. Appropriate ganglionectomy and intraspinal section of the preganglionic innervation minimizes the chances for regeneration.

The prognosis, then for patients after dorsal sympathectomy, is excellent for relief of symptoms providing complete denervation is accomplished. Vasomotor phenomena may persist even in the total absence of sudomotor activity and this fact strengthens the theory of the role played by local faults in the pathogenesis of Raynaud's disease. Prognosis for permanence of relief is apparently improved if a more extensive type of postganglionic sympathectomy is performed, as this will minimize the chance of leaving accessory sympathetic fibers and also will reduce the chance of regeneration of fibers. It is to be hoped that in the future a more radical operation, including excision of the sympathetic trunk, starting at the stellate ganglion, and carried down through the fourth

dorsal vertebra, and intraspinal section of preganglionic fibers, will prove to be associated with more complete and more permanent results. It should be explained to patients about to undergo operation that amelioration of symptoms rather than complete disappearance of symptoms will probably result.

HYPERTENSIVE VASCULAR DISEASE ASSOCIATED WITH RAYNAUD'S DISEASE

Leinwand, Hinton, and Lord[18] have recently reported 2 patients, both white women, in whom quadrilateral Raynaud's disease associated with hypertensive vascular disease was successfully treated by total sympathectomy.

One of the patients in our series, a 51-year-old white man, underwent a bilateral splanchnicectomy and thoracic sympathectomy (eighth to twelfth dorsal vertebrae) on Jan. 11, 1935, for essential hypertension with severe hypertensive headaches. He had had hypertension with quadrilateral Raynaud's disease for 15 years (since the age of 35 years). On March 27, 1935, a bilateral upper dorsal sympathectomy (excision of the first and second dorsal vertebrae) was performed, and on April 11, 1935, a bilateral lumbar sympathectomy (second, third, and fourth lumbar vertebrae) was done. He has been followed through the years because of the subsequent development of carcinoma of the lip, which was successfully treated by excision and a suprahyoid neck dissection. He returned on April 25, 1950 (15 years postoperative), for follow-up study, at which time his hypertension (180/100) was asymptomatic and his Raynaud's disease was completely relieved. In the intervening years these diseases had caused him no trouble. There was no sudomotor activity in the upper extremities and angiospastic activity could be demonstrated only with difficulty.

A second patient, a 52-year-old white woman, suffered from hypertensive headaches prior to bilateral splanchnicectomy and thoracic sympathectomy (eighth to eleventh dorsal vertebrae) on Jan. 17, 1942. Six months after splanchnicectomy she developed a severe type of Raynaud's syndrome in the fingers of the left hand. On Nov. 29, 1942, a left dorsal sympathectomy (second and third dorsal vertebrae excised) was done, followed by complete relief of her Raynaud's symptoms. She returned to the Vascular Clinic in May, 1950, for follow-up study, at which time she was relatively well. She has hypertensive heart disease but no other symptoms relative to her hypertension.

Her Raynaud's symptoms have been cured for 8 years, although she has recently noticed the return of sweating in the left hand.

A third patient, a 36-year-old man who had malignant hypertension, underwent splanchnicectomy on Nov. 16, 1939, with good relief of headaches and other symptoms. He had had hypertension and quadrilateral Raynaud's disease (mild in the feet) since the age of 25 years. No operation was performed for his Raynaud's disease, which did not progress prior to his death Sept. 16, 1945. Autopsy confirmed the diagnosis of apoplexy.

Several other patients in this series had hypertension which was not as severe as in the cases cited. Migraine was also present in some patients with Raynaud's disease. In such cases, the Raynaud's disease appears to be only one manifestation of generalized angiospasm which also manifests itself as essential hypertension or migraine. The prognosis for the Raynaud's disease in this group of cases does not appear to differ from the prognosis in Raynaud's disease in general. The patient's prognosis depends on the severity of the associated hypertension and the response to treatment of the hypertension.

COMMENTS

Very mild forms of Raynaud's phenomenon are very common and do not often come under the observation of physicians. The forms of moderate severity seen by physicians are less common but by no means rare. When confronted

with an early case of moderate severity one cannot prognosticate until it can be ascertained whether that case represents Raynaud's disease or Raynaud's syndrome. This requires the passage of time to be sure that the symptoms are not merely the forerunner of signs of diffuse scleroderma, Buerger's disease, arteriosclerosis obliterans, and other diseases. If involvement does not become bilateral, if ordinarily palpable peripheral pulses become impalpable, or if other criteria are not satisfied to establish a diagnosis of Raynaud's disease, the case must be classed as secondary Raynaud's syndrome. In such a case it is said that prognosis depends upon the underlying pathology (we are now in the process of studying this question). Two years should elapse before a diagnosis of Raynaud's disease is made.

Anyone who has studied a large number of these cases is impressed by the infinite variety of related symptoms and signs and by the fact that immediate diagnosis and prognosis in an early case is fraught with hazard. We have seen Raynaud's symptoms preceded by as long as a year the onset of scleroderma, although the 2 diseases appear to be no more related than are Raynaud's disease and rheumatoid arthritis. The history of overexposure to cold and of chilblains in youth is frequently elicited in patients, especially those who have grown up on a farm. It is sometimes almost impossible to rule out frostbite as the cause of the symptoms. However, if over an adequate time interval the patient presents the symptoms of true Raynaud's disease and the history of frostbite is not overly convincing, then this diagnosis seems justified.

There are 3 clinical types of patients with Raynaud's disease: those whose symptoms are precipitated by cold alone, those in whom both exposure to cold and emotional upsets precipitate attacks, and those who while sensitive to cold have an extremely prominent functional element. In our experience, patients of the first type usually have the least difficulty as avoidance of exposure to cold prevents attacks. Further, they do not often progress to a point at which tissue is lost, providing that they take good care of themselves. The last group has the most difficulty, usually experiencing attacks all through the summer months or in warmer climates. Patients in this group are much more likely to progress to loss of tissue or to dorsal sympathectomy for relief of severe incapacity. Unfortunately, these patients appear to have the poorest postoperative results, regardless of whether sympathetic denervation is and remains complete as shown by tests for sudomotor and pilomotor activity.

The second group just mentioned is in general intermediate in severity between the first and third groups. Thus clinical appraisal of the patient's personality, of his capacity for wide variations in vasomotor activity in response to stress, and of his capability for intelligent cooperation in management is an important aspect in prognostication. We have never seen a patient relieved by psychiatric means but see no reason why skilled psychiatric care would not help those patients with associated evidence of marked vasomotor instability. Certainly, therapy designed to relieve anxiety states in such cases would be well worth while.

The inexact correlation between relief of symptoms in patients undergoing dorsal sympathectomy and the completeness of the denervation has been ob-

served on numerous occasions. While patients with complete anhydrosis of the upper extremities in general are more relieved than patients with only partial anhydrosis, this is not always the case. Among postoperative cases one finds good clinical evidence to support, on the one hand, the theory that Raynaud's disease is due to sympathetic overactivity (Maurice Raynaud) and, on the other hand, that it is due to a local fault in the digital vessels (Sir Thomas Lewis). One cannot escape the impression in still other patients (who have had complete sympathetic denervations of the upper extremities and who have evidence of marked vasomotor instability) that in marked instability of the personality and of the vasomotor system, constrictor influences or substances act upon the digital vessels in the absence of sympathetic innervation. This is regardless of whether dorsal sympathectomy was of the pre- or postganglionic type.

In almost 40 per cent of our cases Raynaud's disease also involves the lower extremities, usually to a lesser degree than the upper extremities. In 2 such cases we have been impressed by the severity of intermittent claudication of the calf muscles as well, and this in the presence of excellent peripheral pulsation.

SUMMARY

In 100 cases of Raynaud's disease diagnosed at the University Hospital in the 12 year period July, 1934, to July, 1946, and in whom follow-up information of at least 5 years has been obtained, there were 77 (per cent) females and 23 (per cent) males. The age of onset was from 11 to 30 years in 60 per cent of cases and from 11 to 40 years in 81 per cent. The duration of the condition and follow-up study was from 11 to 55 years in 85 per cent of cases and from 5 to 55 years in 100 per cent. Obvious vasomotor instability or psychoneurosis was a prominent feature in about 50 per cent of cases and was undoubtedly present in many others. Attacks of Raynaud's disease could be precipitated by exposure to cold in 100 per cent of cases, by emotional upset in 60 per cent of cases, and by either in 60 per cent of cases. Hypothyroidism, mild secondary anemia, allergic rhinitis and other allergies, migraine headaches, and hypertension were not uncommon associated findings in this group of patients. In some women symptoms occurred with or were intensified by the menopause. In these, improvement or disappearance usually followed this period.

PROGNOSIS IN PROPERLY DIAGNOSED RAYNAUD'S DISEASE

a. Of 100 patients, 17 exhibited only slight progression of symptoms over a period of years, in 40 per cent the symptoms remained stationary, and in 12 per cent the phenomenon regressed or disappeared. Thus the prognosis in 69 per cent of cases is for a relatively benign chronic course.

b. Six per cent of the patients exhibited moderate progression to a point short of ulceration or necrosis of the finger tips or to a point where they would submit to dorsal sympathectomy.

c. One-fourth of the cases (25 per cent) progressed to a point at which necrosis, ulceration, or gangrene of the finger tips occurred (11 per cent of total cases), or to a point at which pain and other symptoms were so disabling that sympathectomy was performed. These we have termed severely progressive cases.

Of the 25 per cent of the cases classed as severely progressive the following characteristics are apparent:

a. There is no difference in ratio of females to males as compared to the total series of cases.

b. The age at onset of symptoms was between 11 and 30 years in 17 cases (68 per cent), and over 30 years of age in only 32 per cent of the cases (8 cases). There were no cases beginning in childhood and only 1 case (4 per cent) beginning at over 40 years of age.

c. The rate of progression (duration of symptoms) to tissue loss or sympathectomy was 1 to 4 years in 40 per cent of the cases, 1 to 7 years in 64 per cent, and 1 to 15 years in 92 per cent. Almost every case taking over 10 years to progress to tissue loss or necessity for sympathectomy was characterized by prominent vasomotor instability. This was somewhat less true of cases of less than 10 years' duration, although in this latter group obvious signs of vasomotor instability were more marked than in the entire series as a whole.

d. One cannot therefore, prognosticate on the basis of sex, but one can say that the majority of severe cases will have their onset between the ages of 11 and 30 years and that these will progress to a point of tissue loss or sympathectomy usually within 7 years and almost certainly by the end of 15 years. Cases of over 10 years' duration will probably not advance to such a point unless there is marked clinical evidence of vasomotor instability.

e. Of the patients undergoing dorsal sympathectomy, the great majority will obtain relief for 2 years. There will be recurrences after this time and these will depend somewhat on the technique of operation. It appears that radical postganglionic operations offer a better prognosis for lasting relief than the preganglionic type of sympathectomy.

f. Raynaud's disease associated with essential hypertension has the same prognosis as Raynaud's disease in the absence of hypertension. The patient's outlook depends upon the severity of the hypertension and its response to treatment.

CONCLUSIONS

1. We have proposed the adoption of the terms "Raynaud's disease" and "Raynaud's syndrome" as substitutes for the terms "primary Raynaud's phenomenon" and "secondary Raynaud's phenomenon" in the belief that this will simplify the classification of the disorders under discussion.

2. In 100 patients with true Raynaud's disease of sufficient severity to come to the attention of physicians and in whom the course is known for at least 5 years, one-fourth progressed to a point of tissue loss (ulceration, necrosis, and superficial gangrene) or to a point at which pain and other symptoms caused sufficient disability for the patients to submit to sympathectomy.

3. In most of the remaining three-fourths of the cases the disease ran a benign chronic course for from 5 to 55 years.

4. The one-fourth classified as severely progressive cases were characterized most often by an onset of symptoms between the ages of 15 and 30 years, a rate of progression of under 7 years, or, almost always, by the end of 15 years, and no sex difference.

5. Patients progressing to loss of tissue or necessity for operation usually exhibited other evidence of marked vasomotor instability.

6. Patients whose attacks can be precipitated only by cold or in whom functional factors are not particularly prominent, especially if the onset of their disease is before the age of 15 or after the age of 35 years, are not likely to progress to tissue loss or the need for operation.

7. The majority of patients undergoing dorsal sympathectomy by techniques used in the past will obtain at least temporary relief of symptoms. It is believed that more patients will obtain permanent relief following the radical postganglionic sympathectomies performed at present.

8. Our clinical observations uphold the theory that Raynaud's disease is due both to a local fault in the digital vessels and to superimposed abnormal vasomotor tone. In some cases one or the other of these factors appears to be more prominent.

9. It should be emphasized that the cases included in this study have been subjected to various processess of selection and that the conclusions drawn apply only to classical cases of Raynaud's disease.

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A METHOD OF DEALING WITH ARTERIOSCLEROTIC POPLITEAL ANEURYSMS

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IT HAS been said that aneurysm is one of the few morbid conditions affecting the human being which appears to possess an abiding interest for medical men from generation to generation and century to century.[1]

As the span of life increases, more people are being seen with arteriosclerotic popliteal aneurysms.

The purpose of this paper is to emphasize the efficacy of the method of treatment of this lesion described in 1948 and published in 1949 by Linton[2] before this society, and to report our brief experience with a recent modification of his technique. This method was practiced, in part, by Philagrius of Macedon in the fourth century. It was forgotten until the end of the seventeenth century, when it was used by Purmann.[1]

It is not within the scope of this presentation to review the history of this subject nor the various surgical measures which have been used for this condition. Credit is due to several authors; namely, Mulvihill and Harvey,[3] Bird,[4] Gage,[5] and Richards and Learmonth,[6] who laid the foundation for lumbar sympathectomy followed by extirpation of the aneurysm.

The method to be presented does not differ materially from that of Linton[2] except that in 3 of our cases extirpation of the aneurysm was done immediately after the sympathectomy under the same anesthesia, and that in 1 other case extirpation was done without sympathectomy. Linton[2] has advocated waiting 10 days after sympathectomy before dealing with the aneurysm.

Lilly,[7] as well as Keynes and Morel,[8] has stressed the fact that popliteal aneurysms may be overlooked. It is the duty of the physician to examine carefully the popliteal spaces of patients who come with symptoms usually attributed to "hardening of the arteries." The diagnosis having been made, it is our opinion as well as that of others that lumbar sympathectomy followed by extirpation of the aneurysm is indicated.

The clinical signs of aneurysm are as follows: (1) globular pulsating swelling, (2) distinct thrill and systolic murmur, (3) congestion and edema of the parts beyond, (4) pain and disturbances of sensation, and (5) erosion phenomena. Not all these signs are present in every case.

Patients presenting arteriosclerotic popliteal aneurysms are usually in the older age group and consequently are not considered the best of surgical risks. Provided that the patient is not in cardiac failure and has not a marked hypertension or some associated condition which is likely to terminate fatally, such as carcinoma, lumbar sympathectomy followed by extirpation of the

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aneurysm is advised. Surgical treatment is advised for 2 main reasons: (1) because of the possibility of rupture of the aneurysm, and (2) because of the likelihood of embolic phenomena occluding the distal vessels with resultant gangrene.

A careful history is taken and physical examination is done. The vascular status of both lower extremities is carefully determined. Skin temperature studies may be done. Routine laboratory tests are performed, including determination of Rh and blood group. The estimation of cholesterol, cholesterol esters, fatty acids, and total lipoids provides information of little value in the preoperative evaluation of these cases. Routine roentgenograms of the region of the knee will often show the presence of an arteriosclerotic aneurysm.

Fig. 1, *a* and *b*.—Lateral arteriograms.

An arteriogram gives much more accurate information than the routine roentgenogram. It gives important data related to the size of the aneurysm, its position and the extent of the collateral circulation, and may aid in the differential diagnosis. The patient is placed on a fracture table with the lower extremities abducted. Two portable x-ray machines are placed so that antero-posterior and lateral roentgenograms may be taken almost simultaneously. The patient is given an intradermal test dose of 35 per cent Diodrast. If there is no untoward reaction the patient is anesthetized with Pentothal Sodium and the arteriogram is done. A longitudinal incision is made over the common femoral artery. The latter is isolated with a tape, as is the femoral vein if the latter is readily accessible. Fifty cubic centimeters of the 35 per cent Diodrast are injected into the artery, and the roentgenograms are made.

After the needle has been withdrawn a pledget of Gelfoam is pressed against the opening in the artery until the bleeding has ceased. The incision is closed in layers.

Figs. 1 *a* and *b* and 2 *a* show the type of arteriogram which results. Fig. 2 *b* shows that the popliteal artery was normal and that our clinical impression of an aneurysm of the popliteal artery was wrong.

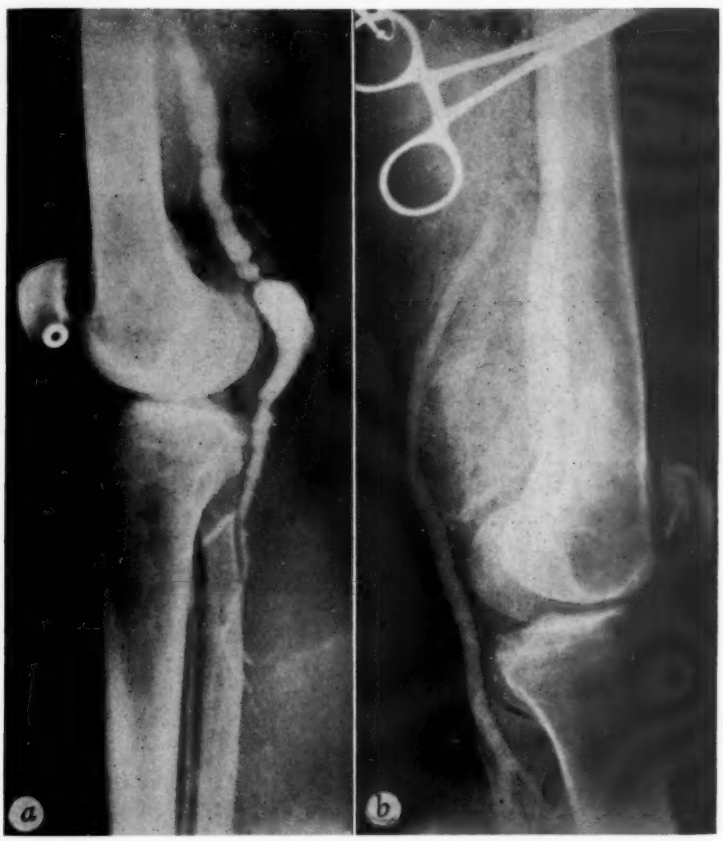

Fig. 2.—*a*, Lateral arteriogram; *b*, lateral arteriogram showing normal popliteal artery. Lower part of femoral artery displaced posteriorly by a mass.

Several days following the arteriogram lumbar sympathectomy is performed. For this portion of the surgical treatment we are indebted to our neurosurgical colleagues. We are especially indebted to Dr. C. S. MacCarty, who has shown particular interest in the neurosurgical aspect of this problem. He uses an S-shaped incision placed anteriorly. The operation is a muscle-splitting procedure. The first, second, and third lumbar ganglia and the sympathetic trunk are approached and removed via the extraperitoneal route.[9, 10, 11] The procedure is not attended with shock and is well tolerated even by elderly patients. The choice of anesthesia is left to the anesthetist.

A popliteal aneurysm may be approached through an adequate longitudinal incision over the line of the artery. By this method, we, like Linton,[2] have had

little difficulty with formation of keloid from a longitudinal incision passing over the crease in the popliteal space. The medial approach advocated by Elkin[12] may also be used. This approach renders more easy the control of the artery proximal to the aneurysm. It is especially indicated when the aneurysm begins in the lower femoral artery. It also saves turning the patient over when the sympathectomy and extirpation of the aneurysm are done under the same anesthetic.

A pneumatic tourniquet placed around the upper part of the thigh is to be used only as an emergency measure. The entire extremity is washed with soap and water, dried with a sterile towel, and prepared with a colorless antiseptic such as aqueous Merthiolate. This allows one to observe the circulatory changes distal to the aneurysm. The limb below the popliteal space is covered with sterile towels, which may be raised to observe the color of the skin. The incision is draped. Great care is used in dissecting free the great nerves, namely, the sciatic, common peroneal, and posterior tibial. After they have been isolated they are retracted with Penrose drains. The popliteal artery is then exposed proximal to the aneurysm. Care is taken not to damage the superior geniculate arteries nor the highest geniculate artery. A tape soaked in saline solution is then placed around the artery proximal to the aneurysm, and gentle traction is applied. The aneurysm is then carefully dissected free from the surrounding tissues. This procedure is rendered more easy by finding the proper cleavage plane. The popliteal vein is usually found to be adherent to the aneurysm and is sacrificed. A tape is then placed around the popliteal artery distal to the aneurysm. We are now ready for the ligation. The proximal artery is doubly ligated and transfixed with number 0 braided silk. Another ligature is placed distal to the foregoing ligatures. The artery is severed between the most distal ligature and one just proximal to it. The severed artery may be dealt with in the manner suggested by Murray and one of us[13] (Janes) by oversewing the cut end of the artery with number 00000 arterial silk on an atraumatic needle. The artery distal to the aneurysm is usually severed between 2 number 0 braided silk ligatures. The aneurysm is then lifted from its bed. The incision is closed in layers without drainage. The skin is closed with interrupted vertical mattress sutures of number 00 black silk. Figs. 3, 4, 5, and 6 show examples of extirpated popliteal aneurysms.

After the incision has been covered with sterile gauze a modified Robert Jones protective dressing is applied from the base of the toes to the groin. The components of this dressing include sterile sheet wadding, sterile absorbent cotton, eider down, and Ace bandages. The main ingredient is the absorbent cotton, which protects the partially ischemic limb. The Ace bandages are loosely applied. (Failure to utilize a protective dressing resulted in 1 case in osteomyelitis of the os calcis due to decubitus. After a long period of morbidity excision of the os calcis was finally performed. The ultimate vascular result, however, has been satisfactory.) The modified Robert Jones dressing by its protective bulk prevents flexion of the knee and obviates the use of a plaster slab or splint.

Postoperatively the foot is cool, but sensation and motion of the toes are hopeful signs. The patient is given 5 per cent alcohol in dextrose intravenously until he can tolerate whiskey by mouth, 2 fluidrams (about 7.4 c.c.) being given every 4 hours. A heat cradle is placed over the trunk. One-half grain (0.032 Gm.) of papaverine is administered every 4 hours. On theoretical grounds these measures should not be necessary as they produce a general vasodilatation. Vasodilatation in the affected limb has already been accomplished by sympathectomy. We have, nevertheless, made use of these means of producing vaso-

Fig. 3.—Extirpated arteriosclerotic popliteal aneurysm.

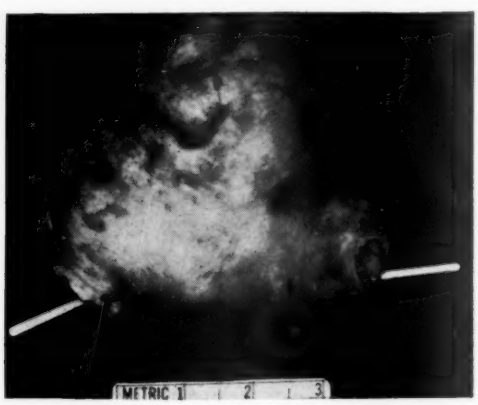

Fig. 4.—Extirpated arteriosclerotic popliteal aneurysm.

dilatation medically. Care is taken not to elevate the limb. The anticoagulants heparin and Dicumarol are not used postoperatively since they are not considered necessary or advisable. The patient is usually ambulatory by the tenth day and uses crutches for an additional 2 weeks. It is not uncommon for the patient to complain of transitory pain in the foot. In all of our cases this has disappeared eventually.

The cases of special interest in this report are included in a total of 42 cases of arteriosclerotic popliteal aneurysms seen at the Mayo Clinic during the

Fig. 5.—Extirpated arteriosclerotic popliteal aneurysm.

Fig. 6.—Extirpated arteriosclerotic popliteal aneurysm.

years 1940 through 1949. One case in which the patient was treated in 1950 has been added for its general interest. In this case the patient was a man 82 years of age, the oldest patient so far treated by the combined procedure.

It is of interest to note that of the total group of 42 patients, 23 (55 per cent) were seen during the last 3 years—1947, 1948, 1949, and to date in 1950. In the entire group there were 41 men and only 1 woman. The youngest patient was 48 years of age and the oldest 88 years of age; the average age was 65.48 years.

One-half of the cases were unilateral aneurysms. Of these 10 were located on the right side and 11 on the left. The remaining 21 cases were bilateral popliteal aneurysms; in one of these there were in addition, bilateral femoral aneurysms; in another there was an aneurysm of the left dorsalis pedis artery, while in another remarkable case there were aneurysms of both iliac arteries and both femoral arteries in addition to popliteal aneurysms.

In 20 cases, representing almost one-half of the entire group, the patients were treated conservatively. In 7 cases (17 per cent) amputation was performed primarily because of arterial insufficiency with impending or frank gangrene. One patient, a 64-year-old white man with a right popliteal aneurysm, was treated by right lumbar sympathetic ganglionectomy and trunk resection alone with good results.

The remaining 14 patients, presenting 15 aneurysms (about 33 per cent of the entire group), were treated by direct surgical attack on the aneurysm itself, with or without sympathectomy, as shown in Table I.

TABLE I. DIRECT SURGICAL TREATMENT OF POPLITEAL ANEURYSMS

SURGICAL TREATMENT	ANEURYSMS
Sympathectomy with extirpation	
Nonsimultaneous	6
Simultaneous	3
Total	9
Sympathectomy with aneurysmorrhaphy	
Nonsimultaneous	4
Aneurysmorrhaphy alone	1
Extirpation alone	1

Three of the patients treated by sympathectomy with subsequent aneurysmorrhaphy obtained good clinical results. The patient, a 61-year-old man with bilateral popliteal aneurysms, underwent amputation 1 month after sympathectomy and 9 days following aneurysmorrhaphy; about 2 years later it was necessary to do a midthigh amputation on the opposite extremity.

The 1 patient treated by aneurysmorrhaphy alone obtained an excellent clinical result. This was a 68-year-old man with bilateral popliteal aneurysms but with symptoms confined to the left lower extremity. Relief was obtained by ligation of the popliteal artery and obliteration of the aneurysm by the Matas technique.[14]

The 1 patient treated by extirpation alone obtained an excellent clinical result and was working steadily 3½ years following his operation. In this

case there was a left popliteal aneurysm in a 57-year-old man with diabetes mellitus and positive serologic reaction. Microscopic examination of the wall of the aneurysm revealed mild arteritis of the nutrient vessels and considerable perivascular lymphocytic cuffing, suggesting a syphilitic etiology. There was also advanced atheromatous change in the vessels.

Of primary concern in this report are the 8 patients, with 9 popliteal aneurysms, treated by extirpation in conjunction with lumbar sympathectomy (Table II). The 6 limbs in which the 2 surgical procedures were not done simultaneously all obtained good results. The convalescence of 1 patient was complicated by osteomyelitis of the os calcis which resulted from a pressure sore on the heel. In 1 case both legs were operated upon, so that a total of 6 extirpations were done on 5 patients in this group. The interval between the sympathectomy and surgical attack on the aneurysm varied from 9 to 60 days.

TABLE II. ARTERIOSCLEROTIC POPLITEAL ANEURYSMS; SUMMARY OF 8 PATIENTS WITH 9 ANEURYSMS TREATED BY SYMPATHECTOMY AND EXTIRPATION

NO.	AGE (YEARS)	INTERVAL BETWEEN PROCEDURES (DAYS)	DATE	RESULTS
1	54	17	1947	Good; returned to work
2	53	11	1947	Good; returned to work
3	48	9	1949	Good; returned to work
4	52	60	1948	Good; returned to work
5	62	L-23	1948	Good; returned to work
6		R-34		
7	63	Simultaneous	1949	Good
8	68	Simultaneous	1949	Good; returned to work
9	82	Simultaneous	1950	Good to date; too recent for final assessment

The 3 patients in whom extirpation of the aneurysm followed immediately on the lumbar sympathectomy likewise had good results. It was considered that a good result had been attained if the patient was able to return to his work or to walk without significant discomfort.

SUMMARY

1. A method of dealing with arteriosclerotic popliteal aneurysms has been presented in detail. This consists of lumbar sympathectomy followed immediately or at a later date by extirpation of the aneurysm.

2. It is evident from our records that increasing numbers of arteriosclerotic popliteal aneurysms are being seen.

3. Surgical treatment is urged before rupture of the aneurysm or embolic phenomena have occurred.

4. Eight patients with 9 arteriosclerotic popliteal aneurysms have undergone lumbar sympathectomy followed by delayed or immediate extirpation of the aneurysm. There were no deaths, and the result was considered good in each case.

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THE SURGICAL MANAGEMENT OF SECONDARY HYPERSPLENISM

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SPLENECTOMY for primary hypersplenism is an established procedure with relatively clear indications, low operative mortality, and, for the most part, satisfactory results. Idiopathic thrombocytopenic purpura and cogenital hemolytic icterus are 2 of the most notable examples of primary hypersplenism. Although the etiology and pathogenesis of the above 2 disease entities are not well understood, the evil effect of the spleen is well known and the beneficial effect of splenectomy is usually observed in both conditions.

During the past decade, Doan and his associates[1] and Dameshek and Estren[2] have called attention to the syndrome of secondary hypersplenism, an overactivity of the spleen occurring in the setting of some primary disease entity. "During the course of a number of diseases, the spleen may become secondarily involved. In a certain proportion of these cases, there develops a syndrome identical with one or other of those already described as primary hypersplenism, in which both specific splenic hypersequestration and compensatory bone marrow hyperplasia may be demonstrated, though there is no familial history of such a trait."[1] Doan[1] classified the cases of secondary hypersplenism into 6 groups, that is, congestive, infiltrative, hemoblastic, inflammatory, neoplastic, and myelofibrotic splenomegaly.

Certain criteria must be fulfilled for the diagnosis of secondary hypersplenism. First, the spleen is enlarged; second, the bone marrow must be normally active or hyperactive; third, there is evidence in the peripheral blood of a reduction below normal of one or more or all of the cellular elements; fourth, there must be some primary disease entity, with involvement of the spleen either directly or indirectly.

What is the mechanism of the spleen's action which leads to the hypersplenic state either in the primary or secondary types? It is at this point that the theories of Doan and Dameshek differ. Dameshek holds that the spleen exerts a humoral effect on the bone marrow which prevents the normal and full maturation of the cellular elements, resulting in a state of deficiency of one sort or another in the peripheral blood. On the other hand, Doan has favored the view that the spleen mechanically and chemically withholds the circulating cellular elements, deplasmatizes them, and "sequestrates" the elements from the blood stream. To quote, "The hypersplenic sequence of events may well include: abnormal stasis within splenic sinuses and/or pulp calling for a compensatory increase in delivery of marrow elements: deplasmatization with increased mechanical intercullar friction; loss of erythrocyte potassium with other electrolyte disequilibria, leading to increased fragility; pathologic concentration of lysolicithin and lysolicithin-like, spherocyte-inducing biochemicals normally produced in physiological amounts by the R-E cells, with hemolytic blocking or

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other polyhemagglutinin antibodies theoretically derivable from the R-E cells, exceptional opportunity for immediate contact phagocytosis by R-E elements; all in all, an ideal environment for the establishment of a vicious cycle of cell withholding and cell destruction capable of acceleration or deceleration, depending upon a variety of factors. The dramatic immediacy of the termination of a true hemoclastic crisis at the operating table, at the moment of ligation of the splenic pedicle, strongly incriminates this inherent, chemicomechanical splenic mechanism.''[1]

Regardless of the theoretical mechanism of the action of the spleen, both Doan and Dameshek recommend splenectomy in a wide variety of disease entities in which there is a clear-cut evidence of secondary hypersplenism from which the patient is suffering above and beyond the effects of the primary disease.

In 1945, Whipple and Blakemore[3, 4] reported on their successful management of portal hypertension by means of shunting procedures between the portal and caval systems of veins. Studies in the Spleen Clinic of the Presbyterian Hospital by Rousselot, Whipple, and their associates[3] had pointed out that splenectomy alone for Banti's syndrome and other types of congestive splenomegaly was frequently disappointing and failed to control hemorrhage from esophageal varices in the majority of cases. It was well known that splenectomy alone in some cases of congestive splenomegaly was curative, but how to select such patients was not clear until Rousselot[5] and Blakemore[4] emphasized the need for direct pressure measurement at the operating table of the pressure in several branches of the portal vein; based on the site of the venous block, a correct decision could be made as to whether a splenectomy alone would suffice or whether a shunt would be necessary combined with splenectomy.

In general, portal hypertension may be caused by an intrahepatic block of the radicles of the portal vein as seen classically in portal (Laennec's) cirrhosis, or by an extrahepatic block due to occlusion of the portal vein itself or an occlusion at some point in the splenic vein. It has been emphasized by Blakemore[4] and Rousselot[6] that the anatomic relation of the coronary vein to the splenic vein and the site of the block is important because splenectomy without a shunt eradicates the esophageal varices when the site of the occlusion of the portal system is on the splenic side of the point of entrance of the coronary vein. On the other hand, a shunt must be combined with splenectomy for a cure when pressure readings show that the coronary vein joins the splenic vein on the splenic side of the point of obstruction.

Many patients suffering from portal hypertension, either of an intrahepatic or extrahepatic origin, show signs of secondary hypersplenism, and much of their incapacity may stem from the effects of an overactive spleen on the peripheral blood, producing usually a pancytopenia but occasionally a -penia of one or the other of the 3 cellular elements.

It is the purpose of this paper to unify the 2 principles outlined previously, that is, (1) the value of splenectomy in cases of secondary hypersplenism, and (2) the need for the measurement, in all cases, of the portal pressure in various points in the portal system, thereby placing on a rational basis the surgeon's

decision whether a splenectomy alone is the procedure of choice or whether a splenorenal shunt should be combined with the splenectomy at the same operation.

Preoperatively, the work-up should include: (1) an evaluation of liver funtion—the following tests have proved useful: bromsulfalein clearance 5 mg./kg.; serum proteins with albumin/globulin ratio; cholesterol and esters; icteric index or serum bilirubin; thymol turbidity; cephalin flocculation; prothrombin; (2) a complete blood count of the peripheral blood, including a platelet count and an evaluation of the platelets in the smear; (3) bone marrow study by aspiration to determine that the marrow is at least normal or hyperplastic; (4) roentgenogram of the chest; (5) renal function studies including a phenolsulfonphthalein test, urinalysis, and blood urea nitrogen, and usually an intravenous pyelogram; (6) an esophagram to determine whether varices are present.

In considering technique, the thoracoabdominal incision as utilized by Carter[7] and Linton and his associates[8] is highly desirable in that it affords excellent exposure of the spleen, splenic vein and artery, the kidney and its pedicle; further, it facilitates the mobilization of the spleen, which is usually adherent to the diaphragm where large collateral venous channels are readily visualized and ligated safely. Venous pressures are measured by means of a Becton-Dickinson manometer using a 3 way stopcock and a Lindemann needle. The pressure is measured in a branch near the splenic pedicle and also in a branch of the coronary vein along the lesser curvature of the stomach. A biopsy of the liver is routinely taken and accessory spleens searched for, as Doan[1] and others have shown that a small accessory spleen may lead to a recurrence of the manifestations of hypersplenism.

To illustrate the management of patients suffering from secondary hypersplenism, 5 typical cases will be presented.

CASE 1.—T. O. (University Hospital K24972), a 55-year-old white woman, was admitted to the hospital on Nov. 3, 1948, complaining of episodes of nausea and vomiting of 11 months' duration, associated with epigastric pain which radiated to her back. In addition there had been a 30 pound weight loss and easy fatigability. The past history was significant only in that a cholecystectomy had been performed 3 years prior to admission. The positive findings on physical examination included slight enlargement of the axillary and cervical lymph nodes, a palpable liver 2 fingerbreadths below the right costal margin, and splenomegaly to the extent of 7 fingerbreadths below the left costal margin. The salient laboratory data are shown in Table I. Examination of the bone marrow revealed it to be normal. An esophagram was negative for varices. The preoperative diagnosis was Banti's syndrome on the basis of an intrahepatic block causing portal hypertension and secondary hypersplenism. Operation consisted in splenectomy through a thoracoabdominal incision, biopsy of the liver, and measurement of the portal pressure. A shunt was not performed because of the relatively mild elevation of the portal pressure. Postoperatively, the patient has been entirely asymptomatic for 18 months and has gained 30 pounds. The postoperative laboratory data are shown in Table I.

Comment.—A proved case of lymphosarcoma of the spleen, hilar lymph nodes, and liver associated with secondary hypersplenism developing in a 55-year-old white woman has been substantially helped by splenectomy. A shunt was not carried out because of a portal pressure only slightly above normal.

TABLE I. LYMPHOSARCOMA (SPLEEN, HILAR LYMPH NODES, AND LIVER), SECONDARY HYPERSPLENISM, PANCYTOPENIA IN A 55-YEAR-OLD WOMAN (CASE 1)

DATE	WEIGHT	HEIGHT	RED BLOOD CELL COUNT	HEMOGLOBIN	WHITE BLOOD CELL COUNT	PLATELETS	SEDIMENTATION RATE 42	CEPHALIN FLOCCULATION	BROMSULFALEIN
11/16/48			2.90	8.7	4,450	130,000		4+	10/45
11/22/48	155		3.65	8.9	3,650		56		
12/ 3/48	Operation: Splenectomy (spleen; 1,530 Gm.; portal pressure, 145 mm. H_2O)								
12/ 6/48 P.O. 3 days			4.51	12.8	9,000	220,000			
12/15/48 P.O. 12 days			3.83	10.4	7,150				
12/20/48 P.O. 17 days		Discharged							
2/9/49 P.O. 2 mo.	155		3.92	10.8	12,050				
11/22/49 P.O. 12 mo.	174	44	3.7	11.6	9,700	385,000			
1/3/50 P.O. 13 mo.	179.5		General condition excellent; asymptomatic						
6/6/50 P.O. 18 mo.	185		4.4	12.5	7,800	asymptomatic		3+	6/45

CASE 2.—E. K. (University Hospital K28055), a 38-year-old Negro woman, was admitted to the hospital on March 23, 1949, complaining of progressive enlargement of the abdomen which caused some vague diffuse discomfort of 1 year's duration. For 3 months there had been moderate exertional dyspnea and for 2 months "red bumps" had appeared on the skin of the trunk and lower extremities. Physical examination showed a middle-aged colored woman with a protruberant abdomen. There were innumerable nodules and dry papules from 2 to 10 mm. in diameter over the skin of the entire body. Auscultation of the chest revealed numerous wheezes and dry râles throughout both lung fields. The blood pressure was 120/80 and the heart was not remarkable. The abdomen was ovoid and there were several striae. An umbilical hernia 4 cm. in diameter was present. The liver was enlarged, extending 4 fingerbreadths below the right costal margin, and the spleen was huge, extending 3 handbreadths below the left costal margin. It was tender and firm. The legs showed a 2 plus pitting edema. The essential laboratory data are shown in Table II. Additional information of note included a skin biopsy which was microscopically typical of Boeck's sarcoid, roentgenograms of the chest showing changes consistent with the diagnosis of Boeck's sarcoidosis, and also cystic changes with periosteal thickening in the long bones. Repeated serologic tests were positive for syphilis, but the Department of Dermatology and Syphilology was skeptical of a syphilitic basis for the positive tests and held that sarcoidosis was responsible for the abnormal findings. Examination of the esophagus was negative for varices and examination of the bone marrow revealed it to be moderately hyperplastic. The preoperative diagnosis was generalized Boeck's sarcoidosis with secondary hypersplenism. Operation was deemed advisable to rid the patient of her large spleen and its secondary effects on the peripheral blood. At operation, a splenectomy was performed for a large spleen which weighed 3,300 Gm., the liver was biopsied, and the portal pressure was measured and found to be 260 mm. of water. The liver was covered with large nodules 2 to 4 cm. in diameter and did not resemble a cirrhotic organ. A splenorenal shunt was contemplated but was not performed for 3 reasons. First, the patient did not have esophageal varices by x-ray and there had been no hemorrhagic episode; second, the elevation of the portal pressure was only moderate and not excessive; third, it was our opinion at the operating table that the patient was not an ideal surgical risk and we did not know how well an in-

TABLE II. BOECK'S SARCOIDOSIS (LIVER, SPLEEN, LYMPH NODES, BONES, LUNGS) IN A 38-YEAR-OLD WOMAN (CASE 2)

DATE	RED BLOOD CELL COUNT	HEMOGLOBIN	WHITE BLOOD CELL COUNT	PLATELETS	SEDIMENTATION RATE (MM./HR.)	CEPHALIN FLOCCULATION	THYMOL TURBIDITY	ICTERIC INDEX	CHOLESTEROL AND ESTERS	SERUM PROTEIN WITH A/G	
3/23/49	2.47	6.9	4,750	100,000	79	4+	4.5	30	105/55	7.7	3.5/4.2
4/25/49	2.9	9.7	4,400	230,000	41						
5/ 6/49	Operation: Splenectomy (spleen, 3,300 Gm.; portal pressure, 260 mm. H_2O)										
5/ 9/49 P.O. 3 days	3.33	10.0	8,750	410,000							
11/30/49 P.O. six mo.	3.83	9.7	8,400	580,000	17				135	7.2	3.6/3.6
4/21/50 P.O. 11 mo.	3.6	11.4	5,150	230,000	10	3+	2.5	37.5	140/65	7.6	3.7/3.9
4/22/50	Exploratory laparotomy; died first postoperative day; autopsy performed										

dividual suffering from generalized sarcoidosis would withstand a long procedure. It was of considerable interest to observe the patient go through a smooth uneventful postoperative course and leave the hospital considerably improved by the twelfth day.

The postoperative data are also shown in Table II. During the next 10 to 11 months, the patient was moderately improved, but at no time was entirely symptom-free. Her chief complaint was a chronic cough. The abdominal discomfort and exertional dyspnea were considerably improved by the operation. For several weeks prior to her second admission, some 11 months postoperatively, postprandial pain had developed, associated with nausea and vomiting of recently ingested food. Examination showed in addition to the large liver extending 5 fingerbreadths below the right costal margin, a mass in the left side of the epigastrium extending to the umbilicus. A gastrointestinal x-ray series showed an extrinsic pressure defect on the greater curvature of the stomach. There was no ascites or peripheral

Fig. 1.—Preoperative esophagram showing well-developed varices.

edema and the skin lesions were barely visible. Laparotomy was decided upon on the basis of a preoperative diagnosis of either a malignancy of the stomach or a huge enlargement of the left lobe of the liver. A small transverse left rectus incision was made and the latter diagnosis confirmed, a biopsy taken, and the incision closed. The operation was simple and, postoperatively, the patient was walking about the ward within 12 hours. Approximately 20 hours postoperatively, without warning, the patient was found dead in bed by the nurse. Autopsy revealed extensive sarcoidosis of the lungs, pleura, lymph nodes, heart, pericardium, trachea, larynx, liver, pancreas, kidneys, breasts, skin, bone marrow, esophagus, stomach, and ileum. An interesting additional finding was bilateral adrenal atrophy involving the glomerulosa layer. No obvious cause of death such as a pulmonary embolus, coronary occlusion, or intraperitoneal hemorrhage was found.

Comment.—Mino and his associates[9] reported an interesting case of a 26-year-old woman with generalized Boeck's sarcoidosis whose most disabling symptom had been ascites. They performed a splenectomy and splenorenal shunt. The spleen weighed 2,250 Gm. and the portal pressure measured 175 mm. of water. Postoperatively, her course was stormy but she went on to a full recovery, suffering only from weakness in the legs, presumably due to spinal cord involvement by the sarcoid process. She remained relatively well until December, 1949, approximately 2 years postoperatively, when dyspnea and vomiting appeared. The patient suddenly died a few days following readmission to the hospital. At no time during the period following discharge from the hospital had ascites reappeared.[10]

Fig. 2.—Postoperative esophagram 3 months later showing clearance of the varices.

These 2 cases of Boeck's sarcoidosis with portal hypertension and secondary hypersplenism had similar courses in that both were benefited by splenectomy, and the patient in whom ascites was present was helped considerably by a splenorenal shunt. That the improvement was only for 1 and 2 years, respectively, points up the serious nature of generalized sarcoidosis in some patients and calls for a guarded prognosis, even though moderate benefit from splenectomy with or without a combined shunt is likely to occur.

CASE 3.—I. S. (University Hospital K28398), a 36-year-old white man, was admitted to the hospital on Jan. 17, 1949, complaining of episodes of fever, upper abdominal pain, nausea, and fatigue of 6 months' duration. (Four years earlier, the patient had had an unexplained massive hematemesis.) There had been a loss of 25 pounds in weight during the 6 months prior to admission. The patient had never been jaundiced and rarely indulged in alcoholic beverages. Physical examination revealed a muscular, well-developed man. The positive findings included splenomegaly 3 fingerbreadths below the left costal margin and tenderness in the epigastrium. The liver was not palpable. Salient laboratory data are shown in Table III. An esophagram showed well-developed varices (Fig. 1). On Jan. 29, 1949, the patient was subjected to a combined splenectomy and splenorenal shunt through a left thoracoabdominal approach. The portal pressure measured 440 mm. of water and the spleen weighed 1,115 Gm. The postoperative laboratory data are also shown in Table III; an esophagram performed 3 months postoperatively demonstrated a complete absence of esophageal varices (Fig. 2). The patient has remained entirely well during the past 16 months with the one exception that he tires easily.

TABLE III. CIRRHOSIS OF LIVER, PORTAL HYPERTENSION, MASSIVE HEMORRHAGE FROM ESOPHAGEAL VARICES, AND SECONDARY HYPERSPLENISM, CHIEFLY THROMBOCYTOPENIA, IN A 36-YEAR-OLD MAN (CASE 3)

DATE	WEIGHT	RED BLOOD CELL COUNT	HEMOGLOBIN	WHITE BLOOD CELL COUNT	PLATELETS	PLASMA PROTEINS	A/G RATIO	CEPHALIN FLOCCULATION	ICTERUS INDEX	BROMSULFALEIN
1/13/49	183	4.01	12.0	5,050	140,000	6.7	4.0/2.7	3+	27 15	26/30 16/60
1/29/49	189	Operation: Splenectomy with splenorenal shunt; (spleen, 1,115 Gm.; portal pressure, 440 mm. H_2O)								
2/2/49 P.O. 4 days		3.95	11.4	9,650	265,000					
2/18/49 P.O. 20 days	171	3.70	11.0	6,200	600,000	5.3	3.0/2.3	1+	8.8	16/60
P.O. 21 days	Discharged									
6/29/49 P.O. 5 mo.	196	4.2	13.6	7,750	265,000			1+		36/30 30/60
12/30/49 P.O. 11 mo.	202	Excellent condition								
4/20/50 P.O. 15 mo.	210	4.37	12.9	7,250	160,000	6.3	4.0/2.3	2+		36/45

Comment.—This probably represents a case of portal hypertension secondary to an extrahepatic obstruction of the portal vein followed by a mild cirrhosis of the liver. The patient has had significant relief of the secondary hypersplenism by the splenectomy and has also had a lowering of the portal hypertension by the splenorenal shunt, as evidenced by the disappearance of the esophageal varices.

CASE 4.—D. McL. (University Hospital K32563), a 12-year-old white girl, was admitted for the first time in June, 1949, with the chief complaint of progressive jaundice of 14 months' duration, developing in a setting of pneumonia treated with one of the sulfonamides. Two months after onset of the jaundice there had been a 10 day episode of right upper quadrant pain, dark urine, and loose stools. Physical examination revealed a chronically ill, undernourished, jaundiced girl with an enlarged liver extending 3 fingerbreadths below the right costal margin and an enlarged, firm, nontender spleen palpable 2 fingerbreadths below the left costal margin. The patient's weight on admission was 76.5 pounds. Table IV shows

the preoperative laboratory data. It was the opinion of Dr. R. Franklin Carter that the patient's biliary tract should be explored for possible extrahepatic biliary obstruction and if none were found, then a cholecystostomy performed. The preoperative diagnosis was a chronic hepatitis with early cirrhosis and portal hypertension. At operation on June 29, 1949, the extrahepatic bile ducts and gall bladder were found to be normal, the liver was enlarged and nodular, and the portal pressure measured 410 mm. of water. A cholecystostomy was performed. The postoperative course was characterized by a gradual deterioration of liver function and increasing jaundice. The patient was discharged on July 30, re-admitted for 4 days on August 23 for a questionable wound infection, and then re-admitted for a splenectomy on Sept. 22, 1949. By the time of the third admission ascites had developed, the icteric index had risen to 180, and all of the liver function tests which were studied showed further impairment. The cholecystostomy was allowed to close by the end of September. Because of the significant signs of secondary hypersplenism and the known portal hypertension of 410 mm. of water, a combined splenectomy and splenorenal shunt were performed on Oct. 28, 1949, after intensive preoperative preparation. The spleen weighed 580 Gm. The postoperative course was remarkably smooth except for a temporary increase in the jaundice, the icteric index reaching 300 on the second postoperative day. By the time of discharge, the icteric index had fallen to 150 and her weight was 85 pounds, which was the same as on admission 2 months earlier.

During the past 7 months the patient's improvement has been progressive and gratifying. Her weight has risen to 110 pounds, and her physician in the Gall Bladder Clinic* has found it necessary to curtail starches and desserts in order to avoid overweight. The jaundice has completely cleared clinically, and liver function has improved moderately. In general, the patient feels well, is free from pain, and does not tire easily. Table IV also shows the postoperative laboratory data.

TABLE IV. CIRRHOSIS OF LIVER, PORTAL HYPERTENSION, ASCITES, SECONDARY HYPERSPLENISM, PANCYTOPENIA IN A 12-YEAR-OLD GIRL (CASE 4)

DATE	WEIGHT	RED BLOOD CELL COUNT	HEMOGLOBIN	WHITE BLOOD CELL COUNT	PLATELETS	PLASMA PROTEINS A/G RATIO	CEPHALIN FLOCCULATION	ICTERIC INDEX	CHOLESTEROL AND ESTERS
6/ 1/49	76.5	3.0	10.0	3.7	150,000	9.5 3.4/6.1		70	95 40
6/29/49	Exploratory laparotomy, biopsy of liver, cholecystostomy (portal pressure 410 mm. H_2O)								
7/14/49						7.3 3.4/3.9	4+	210	
7/29/49 P.O. 1 mo.	82	Discharged						160	
8/26/49									
9/22/49		3.6	11.2			7.2 2.7/4.5	4+	162	200 55
	85	3.1	10.0	4.2	200,000	7.4 3.7/3.7		180	
9/23/49	Cholecystostomy tube removed; ascites present								
10/18/49				3.1	130,000		4+	135	224 86
10/28/49	Operation: Splenectomy with splenorenal shunt (spleen, 580 Gm.)								
10/30/49 P.O. 2 days		3.2	10.4	20.0	120,000			300	
11/ 7/49 P.O. 10 days	85	4.27	12.1	13.9	260,000	5.8 3.0/2.8	4+	250	155 55
11/21/49 P.O. 24 days	88.5	3.75	10.7	9.15	210,000			150	
11/22/49 P.O. 25 days	Discharged, no ascites								
12/21/49 P.O. 8 wk.	92	4.2	12.1	6.85		6.5 3.0/3.5	4+	66	106 66
6/1/50 P.O. 7 mo.	109	3.75	10.7	8.3	240,000	6.9 3.3/3.6	3+	24	232 98

*Dr. Elliott Oppenheim.

Comment.—With the exception of the remarkable case reported by Blakemore[11] of an 18-year-old jaundiced white girl (serum bilirubin, 3.6 mg. per cent), who showed a dramatic reversal of her progressive downhill course following a portacaval shunt, this patient is the only one we know of with intense jaundice and hepatitis who has shown such a profound recovery following the combined splenectomy and splenorenal shunt. The signs of secondary hypersplenism have cleared, and it seems likely that the favorable early result may be due to the elimination of the unfavorable action of the spleen, as much if not more than to the lowering of the portal pressure by the shunt. In view of the persistent evidence of moderate impairment of liver function, the ultimate prognosis must remain guarded.

CASE 5.—R. C. (New York Hospital 510562), a 55-year-old white man, was admitted on May 28, 1949. The patient had experienced 6 massive hemorrhages from esophageal varices between January, 1947, and April, 1948. Each hemorrhage had been so severe that coma usually supervened for several days, multiple transfusions were required, and recovery took from 1 to 2 months on each occasion. For 1 year there had been ascites which required tapping every 2 weeks. The past history was remarkable in the fact that the patient had always eaten well, worked hard and regularly, and was not a heavy drinker. Physical examination showed a well-developed, muscular man looking younger than his stated age. The salient findings were: no icterus, the liver was not palpable, and the spleen extended 2 fingerbreadths below the left costal margin. There was a moderate amount of ascites and a small umbilical hernia. The significant preoperative laboratory data are shown in Table V. A preoperative diagnosis of cirrhosis of the liver, portal hypertension, and secondary hypersplenism was made. On June 4, 1948, a splenectomy was performed through a long left rectus incision and a splenorenal shunt was attempted, but was abandoned because of repeated tearing of the splenic vein. Exposure through the left rectus incision was greatly inferior to the thoracoabdominal approach which I have used during the past 18 months for portacaval shunts as a result of the reports by Carter,[7] Linton[8] and Blakemore.[12] In addition to splenectomy, the vessels along the lesser curvature of the stomach were divided and an omentopexy performed. The portal pressure measured 425 mm. of water and the spleen weighed 650 Gm. The postoperative course was uneventful, and he was discharged on the twenty-second day. The patient continued to require paracenteses every 2 to 3 weeks for 4 months, but then over the next 2 months the ascites cleared and has not returned. There has been a weight gain of 30 pounds since operation, hemorrhages have not recurred, and except for easy fatigability, the patient is well. Periods of nausea which are distressing to the patient occur every few months, but they do not interfere with a satisfactory high protein intake. The postoperative data are also shown in Table V.

Comment.—This patient's benefit must be largely due to the splenectomy and its secondary effects on the portal pressure and hypersplenism. The vessels along the lesser curvature probably reanastomosed in a few months and the effect of the omentopexy is probably limited. It was with great regret that a shunt was not carried out successfully for 2 reasons. First, the esophagram at the third postoperative month showed significant improvement in the varices, but all subsequent esophagrams have failed to show any further significant change. Second, it has been my impression that patients following a successful shunt do better generally than those with splenectomy alone for congestive splenomegaly. Although benefit is obvious in this patient as in others in which a shunt has not been effected (1 patient with a small [3 mm.] splenic vein; 1 patient with a case similar to that under discussion—irreparable damage to

TABLE V. CIRRHOSIS OF LIVER, PORTAL HYPERTENSION, REPEATED MASSIVE HEMORRHAGES FROM ESOPHAGEAL VARICES, INTRACTABLE ASCITES, SECONDARY HYPERSPLENISM, PANCYTOPENIA IN A 55-YEAR-OLD MAN (CASE 5)

DATE	WEIGHT	RED BLOOD CELL COUNT	HEMOGLOBIN	WHITE BLOOD CELL COUNT	PLATELETS	PLASMA PROTEINS A/G RATIO	CEPHALIN FLOCCULATION	ICTERIC INDEX	BROMSULFALEIN
5/28/48	173	3.54	10.2	4.0	10,000	5.5 3.2/2.3	2+	12	20.8/45
6/4/48	Operation: Splenectomy and attempted splenorenal shunt (spleen, 650 Gm.; portal pressures, 425 mm. H_2O)								
6/7 /48 P.O. 3 days		3.87	11.0	6.8	350,000	5.1 3.7/1.4			
6/23/48	158.5	4.72	13.9	4.8	250,000	5.7 2.8/2.9			15.0/45
6/26/48 P.O. 22 days	Discharged								
9/24/48 P.O. 3 mo.	173.5	5.1	15.9	8.0	260,000	6.4 2.6/3.8	3+		29.4/45
P.O. 4 mo.	Ascites cleared.								
4/14/49 P.O. 10 mo.	200	5.2	15.0	7.9		7.3 3.4/3.9			61.8/45
12/19/49 P.O. 1½ yr.	205	4.41	13.5	4.1		6.7 3.3/3.4	3+		22/60
5/24/50 P.O. 2 yr.	208	4.9	15.8	10.0	normal in smear	6.6 3.5/3.1	4+		72/30

No postoperative hemorrhages; no ascites during past 20 months.

the splenic vein requiring ligation and splenectomy alone), I feel that every effort should be made to carry out the shunting part of the combined procedure when it is indicated. As a corollary, the surgeon who is not acquainted with the technique of splenorenal shunts should avoid performing a splenectomy alone for congestive splenomegaly. Almost the only opportunity to carry out a shunt in cases of extrahepatic portal hypertension exists at the time the splenectomy is performed. Only with the greatest good fortune is one able to carry out a shunt subsequent to splenectomy in such patients.

SUMMARY

The concept of secondary hypersplenism has been well developed by Doan and Dameshek and their associates and deserves wide recognition. The use of splenectomy in properly selected cases is frequently followed by worth-while improvement, though temporary in some instances. The study of the peripheral blood may show one or more of the cellular elements to be depressed and, in the presence of an active or hyperactive bone marrow, points to the possibility of improvement following splenectomy, although the course of the primary, basic disease entity may not be influenced significantly.

Blakemore, Whipple, and Rousselot have developed satisfactory shunting procedures for the relief of portal hypertension whether on an intrahepatic or extrahepatic basis. In patients with secondary hypersplenism due to a congestive splenomegaly (that is portal hypertension), great benefit may be derived by a combined splenectomy and splenorenal shunt.

It has been the purpose of this paper to integrate the previous 2 developments into a program for the surgical management of secondary hypersplenism. Five illustrative cases have been presented.

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EXPERIMENTAL STUDIES OF THE FROZEN HOMOLOGOUS AORTIC GRAFT

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EVER since the development of successful techniques for suturing blood vessels during the close of the last century, a need has been recognized for a successful method which would allow bridging of large defects in major arteries. In 1896, Jaboulay[1] reported experiments on the transplantation of arterial segments in animals, and a few years later Gluck[2] and Exner[3] reported their studies of venous grafts. Unfortunately, the outcome of these experiments was unsuccessful because of infection, thrombosis, or hemorrhage. However, the subsequent work of Höpfner,[4] Stich and associates,[5, 6] Levin and Larkin,[7] Carrel,[8-12] and Guthrie and associates,[13, 14] demonstrated that success could be achieved with the use of vessel segments. These experimental studies included the use of autologous, homologous, and heterologous grafts, both in the fresh state and preserved by various methods. Certain conclusions derived from gross and microscopic studies in connection with this pioneering work have stood the test of time.[10, 14] It was demonstrated, for example, that autografts, vessel segments transplanted in the same individual, gave by far the most satisfactory results from the standpoint of function and histologic alteration. On the other hand, heterografts, or segments derived from animals of a different species, caused a considerable tissue reaction in some instances and were for the most part the least satisfactory of those studied. The homologous graft, or the vascular segment derived from another member of the same species, has consequently long held a promise of clinical usage, since it was quite evident that autografts are not readily available for satisfactory substitution in large defects of the aorta.

Although Carrel[9-12] had a certain degree of success in the first 2 decades of the century with preserved grafts maintained by refrigeration, employing various types of media, during the past few years Gross and associates[15-17] have developed a technique of refrigeration that has yielded a very high percentage of success in both experimental and clinical application.

With this technique, segments of the aorta and major arteries are obtained aseptically within 6 hours of death and are then stored in a refrigerator at 4° C. in a balanced salt mixture resembling Tyrode's solution, which contains antibiotics, homologous serum, and an indicator for the regulation of the pH. The viability of certain cells in preserved animal grafts has been established by means of tissue culture for periods ranging up to 6 weeks.

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While it is well appreciated that a technique has been developed which does permit the successful correction of certain lesions of the aorta, there are some practical aspects of this technique which seem to demand that a search for a more simple method of preservation be continued.

Establishment of a vessel bank by this method entails a considerable expense for equipment and personnel. The services of well-trained individuals are necessary since there must be a frequent check of sterility, acidity, and temperature, if not of viability. As a result of the experimental studies by tissue culture, segments preserved by this technique have been discarded after 5 or 6 weeks, since it has been felt, if not proved, that viability of the graft is to be desired. Until there is a high degree of cooperation by the pathology departments of hospitals, the local medical examiners or coroners, and the public in general, it is evident that it will continue to be difficult to maintain an adequate supply of vessels in a bank for some time to come. These facts make it evident further why this method does not lend itself to use in the smaller hospitals or in the average community. The maintenance of a vessel bank* in New York City, planned very much like the one of Gross and his associates, has been rather difficult to date despite the participation of a large number of local hospitals in its management.

In view of these points, we have been investigating various methods of preservation which permit storage of vascular segments for much longer periods of time and in a simpler manner. It is most desirable that the functional result and ultimate degenerative changes should be at least comparable to those obtained with segments preserved in a nutrient medium by refrigeration. Because of the conflicting results of the few reported studies of frozen vascular[18-20] segments, we have investigated further this method of preservation. The present report is concerned chiefly with the early results obtained by this method, since observation over a few years is planned in order to evaluate the late findings.

METHOD

Preparation and Storage of the Grafts.—Employing sterile technique comparable to that of a clinical operating room, we have obtained segments of thoracic and abdominal aorta immediately after death from healthy adult mongrel dogs. Generally, between 4 and 6 segments have been obtained from each animal, the length ranging from 1.5 to 3 cm. After careful removal of perivascular fat and the adventitia of the segment, the branches have been ligated flush with the wall of the graft using 0000 braided silk. The segments were then rinsed in physiologic saline solution containing 1,000 units each of penicillin and streptomycin per cubic milliliter at 26° C. The segment was then placed in a sterile Pyrex test tube in an environment of air. The tubes were hermetically sealed with rubber stoppers and a coating of paraffin.

Freezing was accomplished in all instances by immersing the tube into a mixture of solid carbon dioxide ice and 95 per cent ethyl alcohol for 15 min-

*Operated under the auspices of the New York Society for Cardiovascular Surgery and supported by a grant from the New York Heart Association. A detailed description of this unit will be published by Dr. E. C. Keefer and associates.

utes. Repeated checks revealed the temperature of this mixture to be −72° C. However, before the freezing process, 1 group of segments was placed in ice water baths at 3 to 4° C. for a period of 5 to 15 minutes, whereas another group was placed immediately into the mixture of solid carbon dioxide ice and alcohol.

The vessel grafts which have been used in the animals to be reported have been stored for from 1 day to 8 months. Storage has been carried out by 2 methods. One set of vessels has been transferred immediately after quick freezing to a commercial deep freeze unit in which the temperature has been maintained at −27° C. The other set of vessels has been transferred immediately to a heavily insulated box in which the temperatures have been maintained from −60 to −70° C. by solid carbon dioxide ice.

At the time elected for implantation of these grafts into other dogs, the segments have been thawed by 2 methods. Certain grafts have been thawed rapidly by immersing the tubes in a water bath maintained at 35° C., whereas others have been thawed slowly by immersing the tubes in an ice water bath at 4° C. for approximately 5 minutes and then at a room temperature of 26° C.

Technique of Implantation.—Forty-three aortic grafts were implanted into the abdominal aorta of recipient adult dogs. The series was divided into 2 groups: (1) 35 grafts stored at −27° C., of which 13 were implanted into dogs which received anticoagulant drugs postoperatively and 22 into dogs which received no such drugs, and (2) 8 grafts which were stored at below −60° C., of which 3 were in dogs receiving anticoagulant drugs postoperatively and 5 in dogs which received no such drugs.

We employed strict sterile technique throughout and used intravenous Nembutal supplemented by inhalation of ether for surgical anesthesia. The abdominal aorta was exposed through a long midline abdominal incision, by carefully packing the intestinal contents cephalad and to the right side of the abdominal cavity. The abdominal aorta was mobilized from its bed by division of the branches arising from the level of the renal arteries to the bifurcation of the aorta. Both lumbar sympathetic chains from the second to fourth lumbar vertebrae were removed in anticipation of possible danger from hindquarter paralysis and edema. With the selected graft completely prepared for implantation, the aorta was occluded with a special rubber-shod screw clamp,[21] while occlusion of the iliac arteries and mid-sacral arteries was effected by rubber loops. A segment measuring 1.5 to 3 cm. in length was then removed from the isolated segment of abdominal aorta, and a thawed graft of comparable length implanted, using a continuous everting mattress suture of 00000 braided Deknatel arterial silk (Fig. 1). The posterior suture line was completed before the anterior row, and the proximal anastomosis was finished before the distal one, requiring a period of total occlusion of from 30 to 40 minutes. No hindquarter paralysis resulted from this period of aortic occlusion, although we did not employ any method of intubation temporarily during anastomosis which is generally required while working on the thoracic aorta. In 2 dogs a delayed hindquarter paralysis did occur on the fifth postoperative

day in dogs which had received no anticoagulant drugs, as the result of sudden occlusion by septic thrombosis.

Anticoagulation.—In the animals selected for study with anticoagulant drugs, 10 mg. of heparin in a 1 ml. volume of saline solution were injected into the aorta proximal to the graft at operation, prior to restitution of blood flow.

In order to continue anticoagulation for a longer period of time we have given Dicumarol to each of these animals the day of operation, after obtaining a control prothrombin time. Interestingly enough, of the 16 animals so treated in both groups, the control prothrombin times have ranged between 6 and 9.3 seconds with an average of 7.8 seconds. The normal human prothrombin time, determined in the same laboratory, was 13 to 14 seconds.

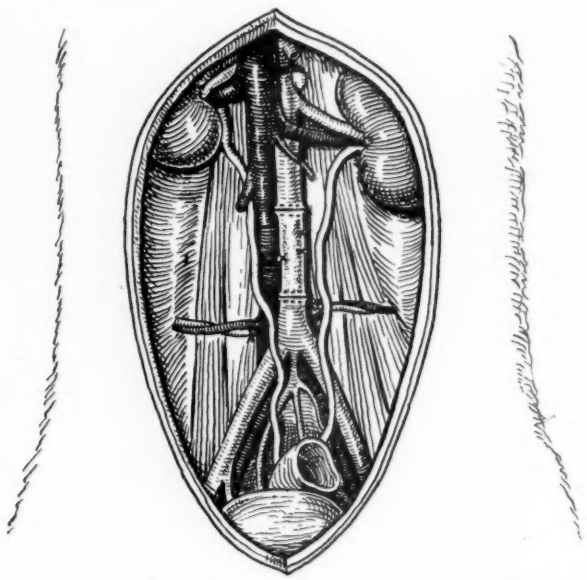

Fig. 1.—Sketch of the aortic graft implanted in the recipient abdominal aorta.

The initial dose of Dicumarol was generally 25 mg. orally. The amount of drug required postoperatively had to be determined by daily determination of the prothrombin time since many of the dogs were either hypo- or hyper-reactors. In general, a dosage of 1 mg. per kilogram of body weight of Dicumarol was sufficient to keep the prothrombin time within the desired therapeutic range of 25 to 50 seconds. Some animals required the drug only 3 days because of marked hyper-reactivity, whereas others were given Dicumarol for 16 days. The average time of treatment with this drug was 9.8 days. We endeavored to keep the prothrombin time above 25 seconds, especially during the first postoperative week. There were no deaths as a result of the therapy in this group, although severe bleeding from the wound in a few dogs had to be treated with fresh blood transfusions and administrations of intravenous vitamin K.

Methods of Studying the Implanted Graft.—Postoperatively, function of the graft was evaluated daily by careful examination of the pulsation in the

femoral arteries, and at varying intervals by aortogram. These were obtained satisfactorily by exposing a single film exactly 7 seconds after beginning a very rapid injection of 15 to 25 c.ml. of 70 per cent Diodrast into the external jugular vein (Fig. 2).

Of the 43 dogs in the entire series, 17 are being allowed to survive for long-term studies. This group has been followed for periods up to 10 months from the time of implantation, and appears to have good function of the graft in all instances. The grafts in 26 animals were studied immediately post mortem (Table I). In the dogs which have been killed, the graft was exposed by sterile operation with the animal under anesthesia. After careful dissection, the intact graft with the adjacent portions of the recipient aorta was removed to allow study by (1) tissue culture, (2) photographs of the gross specimen, and (3) histologic preparation.

Fig. 2.—Aortogram 5 months after the implantation of a frozen graft preserved at -27° C. into the abdominal aorta of a dog which had received anticoagulant therapy postoperatively.

Tissue culture studies: A special laboratory has been equipped to carry out carefully controlled tissue culture studies of the vessel segments preserved by this and other methods. The physical requirements of such a laboratory are very exacting, as are the techniques which must be employed to obtain satisfactory results.[22] All the studies of this type were carried out by one of us (M. S. P.), employing a modification of the technique in which the cultures are grown in Carrel flasks.[23]

TABLE I

RECIPIENT DOG		ANTICOAGULANT DRUGS	DATE OF IMPLANTATION	AGE OF GRAFT (DAYS)	TIME GRAFT IN DOG (DAYS)	CAUSE OF DEATH	RESULTS
Results With Frozen Grafts Stored at –27° C.							
1.	226	+	9/19/49	6	299	Still alive	Excellent function
2.	270	+	9/26/49	10	292	Still alive	Excellent function
3.	224	+	9/30/49	1	288	Still alive	Excellent function
4.	283	0	10/21/49	3	267	Still alive	Excellent function
5.	248	+	10/24/49	25	264	Still alive	Excellent function
6.	269	0	10/26/49	16	262	Still alive	Excellent function
7.	201	0	10/28/49	10	260	Still alive	Excellent function
8.	213	+	10/31/49	32	258	Still alive	Excellent function
9.	254	0	11/11/49	31	246	Still alive	Excellent function
10.	275	+	12/ 2/49	23	225	Still alive	Excellent function
11.	292	+	12/12/49	30	214	Still alive	Excellent function
12.	253	0	12/14/49	30	212	Still alive	Excellent function
13.	430	0	5/10/50	240	66	Sacrificed	Thrombosed completely
14.	528	+	9/16/49	3	10	Hemorrhage	Two small mural thrombi; excellent function
15.	276	0	10/ 5/49	6	5	Hemorrhage; septic thrombosis	Thrombosed completely
16.	204	0	10/ 7/49	2	4	Hemorrhage	Thrombosed completely
17.	298	0	10/31/49	14	9	Bowel obstruction; pneumonia	Small mural thrombus; excellent function
18.	232	0	11/ 2/49	23	7	Sacrificed	No thrombus; excellent function
19.	222	+	10/ 3/49	14	39	Sacrificed	No thrombus; excellent function
20.	286	+	9/28/49	2	58	Sacrificed; pneumonia	No thrombus; calcification of media; excellent function
21.	228	0	11/25/49	30	7	Sacrificed	Thrombosed completely
22.	246	0	11/25/49	30	14	Sacrificed	Small mural thrombus; excellent function
23.	299	+	11/21/49	30	21	Sacrificed	Small mural thrombus; excellent function
24.	212	0	12/21/49	64	13	Sacrificed; pneumonia	Minute mural thrombus; excellent function
25.	281	+	11/28/49	41	44	Sacrificed	No thrombus
26.	297	0	11/ 7/49	12	90	Sacrificed	No thrombus; small intimal erosion in midgraft; excellent function
27.	203	+	1/10/50	90	30	Distemper	Thrombosed completely
28.	240	0	1/27/50	14	14	Sacrificed	Mural thrombus; good function
29.	438	0	2/10/50	93	2	Strangulated bowel obstruction	Minute mural thrombus; excellent function
30.	247	0	10/19/49	1	11	Sacrificed	Thrombosed completely
31.	433	0	2/15/50	135	12	Sacrificed	Small mural thrombus; excellent function
32.	284	0	12/12/49	31	78	Sacrificed	No thrombus; excellent function
33.	258	0	12/29/49	48	62	Sacrificed	No thrombus; small erosion in midgraft covered by endothelium; excellent function

TABLE I—CONT'D

RECIPIENT DOG		ANTICOAGULANT DRUGS	DATE OF IMPLANTATION	AGE OF GRAFT (DAYS)	TIME GRAFT IN DOG (DAYS)	CAUSE OF DEATH	RESULTS
34.	233	0	12/13/49	90	90	Sacrificed	No thrombus; intimal sclerosis
35.	497	0	4/14/50	180	60	Sacrificed	Thrombosed completely
			Results With Frozen Grafts at −60° to −70° C.				
1.	435	0	2/23/50	35	7	Sacrificed	Small mural thrombus; erosion in midgraft; excellent function
2.	476	0	2/24/50	42	14	Sacrificed	Small mural thrombus; excellent function
3.	310	+	6/15/50	120	4	Hemorrhage	No thrombus; Dehiscence of suture line
4.	496	+	2/ 1/50	13	164	Still alive	Excellent function
5.	677	+	2/ 7/50	25	158	Still alive	Excellent function
6.	302	0	5/31/50	105	45	Still alive	Excellent function
7.	304	0	6/14/50	120	31	Still alive	Excellent function
8.	317	0	6/20/50	13	25	Still alive	Excellent function

Aortic tissue to be planted was handled aseptically in a glass hood; the adventitia and the outer portion of the media were discarded in all instances, so that only the inner portion of the media and intimal portion of the vessel were cultured. This technique was employed with these grafts in order to avoid a false positive growth which might be obtained from adjacent normal tissue of the recipient animal in the case of implanted grafts. This inner portion of the vessel so isolated was then divided carefully into small squares approximately 1 mm. on a side and planted in Carrel flasks, 16 colonies per flask, in a thin layer of 1 part chicken plasma to 2 parts Simms X6 solution (Fig. 3). When the plasma had clotted, 1.1 ml. of homologous serum in X6 solution, usually 1 part to 2, was added. The pH was adjusted to 7.2 to 7.8 with sterile CO_2—air mixtures. After a week, the fluid was renewed at intervals with a more dilute solution of homologous serum containing ox serum ultrafiltrate. Observations under low- and high-power magnification were carried out daily for 1 to 6 weeks. Positive results we have recorded here refer to the entire specimen rather than to the individual colonies derived from such a specimen. Consequently, if growth of cells was observed arising from any of the colonies in a single flask, the original segment then was classified as having viability. The actual amount of growth obtained from any segment was determined quantitatively and will be reported in a separate publication, as will the details of the method and the results.

By this method 64 segments of fresh normal aorta were cultured, 27 aortic grafts stored at either −27° C. or −60° C. were cultured after thawing at the time of implantation, and 16 of the implanted grafts were cultured at the time of removal from the recipient animal. In this latter group the excised sterile graft and adjacent normal aorta were opened by vertical incision in order to examine the lumen for evidences of degeneration or thrombus. At this time a 2 to 3 mm. strip was removed from the edge and kept sterile for

tissue culture. In most instances separate cultures were made of the normal aortic ends as well as the proximal, middle, and distal thirds of the graft.

Examination of the excised graft: As previously mentioned, the graft was opened immediately after excision and examined closely for thrombus formation as well as for areas of degeneration. The latter are generally evidenced by areas of erosion on the intimal surface or subintimal deposits of lipoid material or even calcium. In addition, the suture lines were examined closely to determine the character of healing at the anastomosis. Of interest was the amount of suture material evident, and the degree of endothelization as well as constriction. After gross inspection the graft was pinned to a cork board and photographed with appropriate labels.

The mounted graft was then immersed in Bouin solution for up to 48 hours and then transferred to 80 per cent ethyl alcohol. After fixation, a longitudinal strip was cut for imbedding, including the entire graft and adjacent normal aorta. All of the grafts so studied were stained by hematoxylin and eosin, trichrome connective tissue stain, and Verhoeff elastic tissue stain. Sixteen normal control sections of aorta were studied this way as well as 35 frozen grafts after thawing. Of these, 25 were stored at −27° C. and 10 were stored at below −60° C.

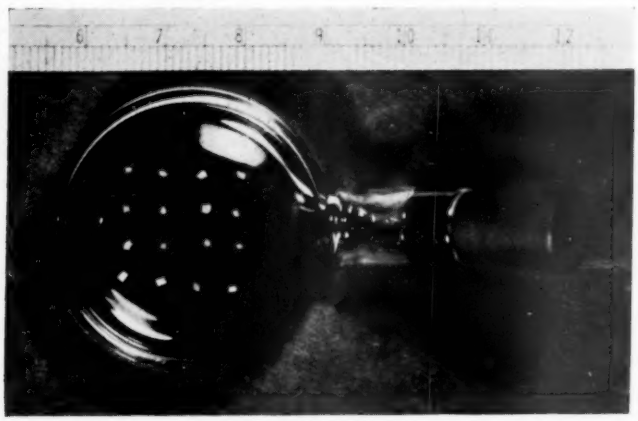

Fig. 3.—Carrel flask containing 16 colonies prepared from an aortic segment of a dog.

RESULTS

Functional Status of Graft.—The palpation of femoral pulses has in general been a fairly reliable index of functional success with the graft in the abdominal aorta. This was carried out daily for several weeks following operation and frequently thereafter. It should be mentioned, however, that in 1 dog in which faint femoral pulsations were felt 3 weeks after the graft had been implanted we found the graft to be completely thrombosed at autopsy. An aortogram ante mortem confirmed the presence of a tremendously developed collateral circulation. There was no instance, however, in which a significant degree of thrombosis was present without definitely modifying the character of the femoral pulse. Aortography was carried out as soon as possible in any animal which had some alterations in the palpable pulse.

These films have also enabled us to determine the degree of constriction present at the suture line as well as the degree of dilatation present in the graft. Minor degrees of constriction were not uncommon and were probably the result of employing a continuous everting mattress suture in relatively small vessels where the inside diameter was generally no more than 3 to 4 mm. The degree of constriction was never sufficient to suggest alteration in amount of blood flow, however (Fig. 2). It has been shown by Mann and associates[24] that there has to be a reduction in the internal diameter of a vessel greater than 70 per cent before one encounters a decrease in blood flow of 50 per cent, and a reduction of 40 per cent in external diameter may be observed without any appreciable change in blood flow. By aortogram, a minor degree of dilatation of the graft was apparent in some dogs. However, there were certain animals in which the diameters of the graft and recipient aorta could not be matched exactly. It was found by experience that a graft of very slightly smaller internal diameter gave the best results insofar as appearance by artogram later. By strapping a calibrated lead marker to the back of the animal at the time of aortography, it was possible to get exact measurements of the graft without sacrificing the animal. In a few animals in which the palpation of the femoral vessels had suggested no abnormalities of function, the aortogram suggested the presence of a small mural thrombus. The presence of these in a certain number of animals was confirmed by post-mortem examination of the graft, but in no instance did they interfere with the function of the graft in specimens which had been implanted a month or more. It was felt that endothelization of the thrombus which had occurred during this period prevented further extension of the thrombosis.

An analysis of these observations on function of the graft has allowed devision of the dogs into 1 group in which no significant obstruction to free flow through the graft was present, and another group in which the graft was closed by thrombosis (Table II). Of the 22 animals with grafts which had been stored at −27° C. and which had received no anticoagulant drugs, a satisfactory function was observed in 16, or 73 per cent. Complete occlusion was found, on the other hand, in 6 specimens, or 27 per cent. Regarding the complete occlusion found in 6 animals in this group, it was felt that some instances were related to infection, even though penicillin was given parenterally for 5 to 7 days postoperatively. In 2 thrombosed grafts examined bacteriologically, positive cultures grew *Staphylococcus albus* in one, and *Escherichia coli* in the other. The presence of a Welch bacillus was suspected in still another animal, but not proved. Of 16 grafts examined post mortem, small mural thrombi were found in 6 instances. With the use of anticoagulant drugs in a somewhat smaller group of animals, it was found that full function was present in 12 grafts, or 93 per cent, whereas only 1 graft, or 7 per cent, was occluded by thrombosis. It should be explained that the animal with the thrombosis in this group had received what must be considered an inadequate amount of anticoagulant drugs for only 3 days and the prothrombin time remained well below the desired therapeutic level.

TABLE II. THE INCIDENCE OF OCCLUSION OF FROZEN GRAFTS BY THROMBOSIS

STORED AT −27° C.								STORED AT −60 TO −70° C.							
NO ANTICOAGULATION				ANTICOAGULATION				NO ANTICOAGULATION				ANTICOAGULATION			
NO OCCLUSION		COMPLETE OCCLUSION		NO OCCLUSION		COMPLETE OCCLUSION		NO OCCLUSION		COMPLETE OCCLUSION		NO OCCLUSION		COMPLETE OCCLUSION	
PER CENT	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT	NO.
73	16	27	6	93	12	7	1	100	5	0	0	100	3	0	0

Of the 6 grafts which were examined at autopsy from this group of dogs receiving anticoagulant drugs, there were only 2 with small mural thrombi, covered by endothelium.

Of the group of 8 dogs in which grafts stored at −60 to −70° C. were placed, there was found no instance of complete thrombosis whether or not anticoagulation had been carried out. In the group receiving no anticoagulant drugs, 2 minute mural thrombi were observed at autopsy.

Gross Characteristics of the Graft.—At the time of excision from the host animal, the fresh normal segment of aorta appeared elastic and pink in color. The slight residual adventitia left on the graft at the time of freezing had the physical qualities of normal loose fibrous tissue with sharp delineation into distinct sheets of cells. Once the test tube containing the graft was immersed into the freezing mixture, the segment contracted slightly and became rigid within a matter of seconds. When placed in the carbon dioxide ice chamber, these tubes became heavily frosted and the graft retained its frozen appearance with very little water loss apparent grossly in the bottom of the tube. The vessels maintained at −27° C., however, did have a progressive slow loss of water which collected eventually as ice at the bottom of the test tube. In addition, the adventitia altered slowly to give the appearance of a slightly glairy layer. So far, the variation in the method of handling the graft before immersion into the freezing mixture has had no obvious effect on the appearance of the graft during storage or after storing.

Once thawed, the segment which had been maintained at −60 to −70° C. appeared slightly less elastic and slightly thinner walled than normal vessels. In addition, the color was very pale pink to flat white. The inner surface of the graft did not appear significantly changed grossly, but the adventitia appeared somewhat viscid, and less easily identified as clearly defined areolar tissue. A more marked difference was observed after thawing the graft which had been maintained at −27° C. These vessels seemed still less elastic and definitely thinner walled than normal vessels, although they all sutured well. It should be noted that of the entire group of frozen grafts, only 1 graft failed by virtue of a dehiscence at the suture line (Table I). This graft was a thoracic aorta from a puppy implanted into an adult abdominal aorta, after storage 4 months at −60° C. Additional experience has shown us that puppy aorta tends to be more friable than adult tissue. The color of these grafts was generally dead white. While again the internal portion of the vessel

grossly did not reveal much change, the adventitia had become viscid. Notwithstanding, it was quite easy to remove this tissue from the distinct layer of media.

Fig. 4 *A*.—Grafts which had been stored at -27° C. for 30 days and removed 30 days after implantation into a recipient dog which had received anticoagulant drugs. There is a post-mortem thrombus in the orifice of a lumbar vessel.

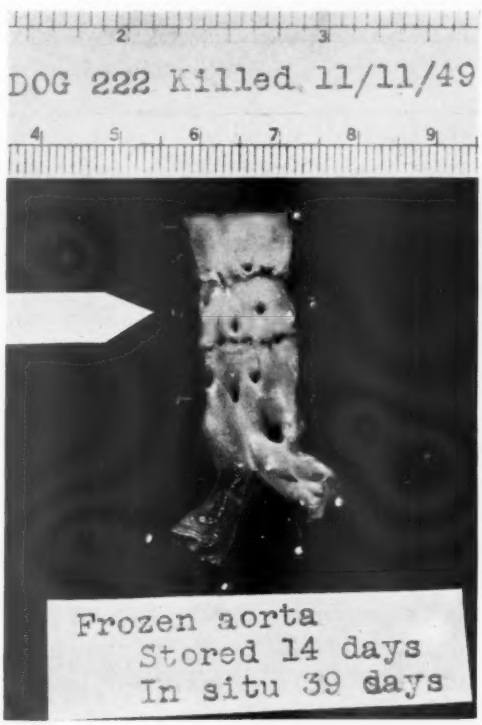

Fig. 4 *B*.—Specimen which had been preserved at -27° C. and was removed 39 days after implantation in a dog which had received anticoagulant drugs.

The first death in our group of animals occurred from hemorrhage when a lumbar branch of the graft blew out. During the early part of this work it was not uncommon for the operator to manipulate the graft by traction on lumbar vessels. Since abandoning this practice there were no other deaths by hemorrhage from this cause. A conscious effort was also made throughout

to avoid pinching the vessel, particularly the intima, with forceps during the process of anastomosis, since it was felt that this trauma contributes to the formation of thrombi. It cannot be denied, however, that a disproportion in luminal diameters contributes as well to the chance of thrombosis. This undoubtedly occurred in the few animals where it was necessary for us to employ a thoracic aortic graft in the abdominal aorta and where a minor degree of discrepancy existed.

Post-mortem studies of the transplanted grafts have been carried out in 26 dogs. Grafts so studied had been implanted in recipient animals for from 2 days to 3 months. As noted before, in animals that were killed the graft was exposed ante mortem using sterile technique. Within hours of the implantation the graft was found invested in inflammatory-like adhesions. This reaction increased and after a few weeks the graft was heavily supported by a thick layer of new fibrous tissue. At the present time we do not feel that this reaction is all the result of tissue immunologic reaction, or that it is due to a

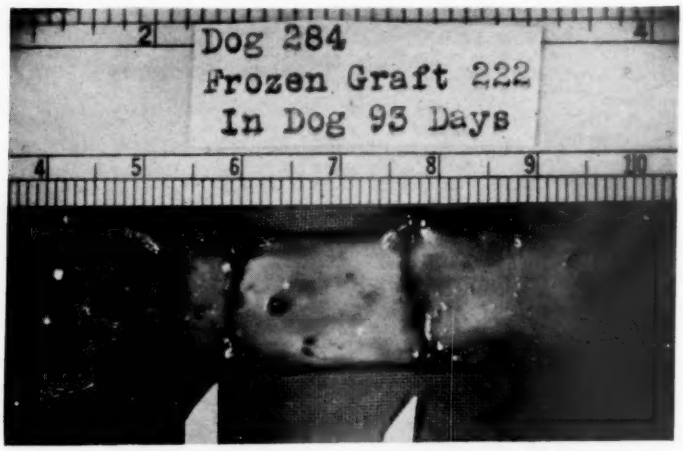

Fig. 4 *C*.—Graft removed 3 months after implantation. The segment had been stored 30 days at -27° C. This dog received no anticoagulant drugs.

foreign body effect, since a similar investing is noted when autografts are employed. When the surrounding adhesions are dissected away, the graft itself has appeared white, tough, and thinner than the adjacent normal aorta, although not appreciably thinner than at the time of implantation. The minor degree of dilatation in a few of the grafts as shown by aortogram was confirmed at necropsy, but there was no formation of aneurysm. In a large number of the anastomoses there was found the minor degree of constriction at the silk suture line, also evidenced by the aortogram (Fig. 2). Up to a week or 10 days the inner surface of the graft may appear somewhat discolored in patchy areas at necropsy, from being stained by hemoglobin post mortem. These areas grossly and microscopically appear to be free of endothelium, which appears to advance from each end. We are carrying out experiments investigating the rate and pattern of re-endothelization of these grafts, but it appears that up to 2 weeks or so is necessary for this process, particularly in

the longer grafts that we have employed. Once covered with endothelium, the surface appears shiny and smooth except for occasional pits marking the orifices of small branches which had been tied when the graft was obtained. The suture line similarly is well covered, although in a number of instances a few millimeters of silk can be observed at various points of the suture lines, lying in a vertical direction. In some of these, observations at the time of anastomosis had revealed absolutely no silk showing. It is felt, therefore, that

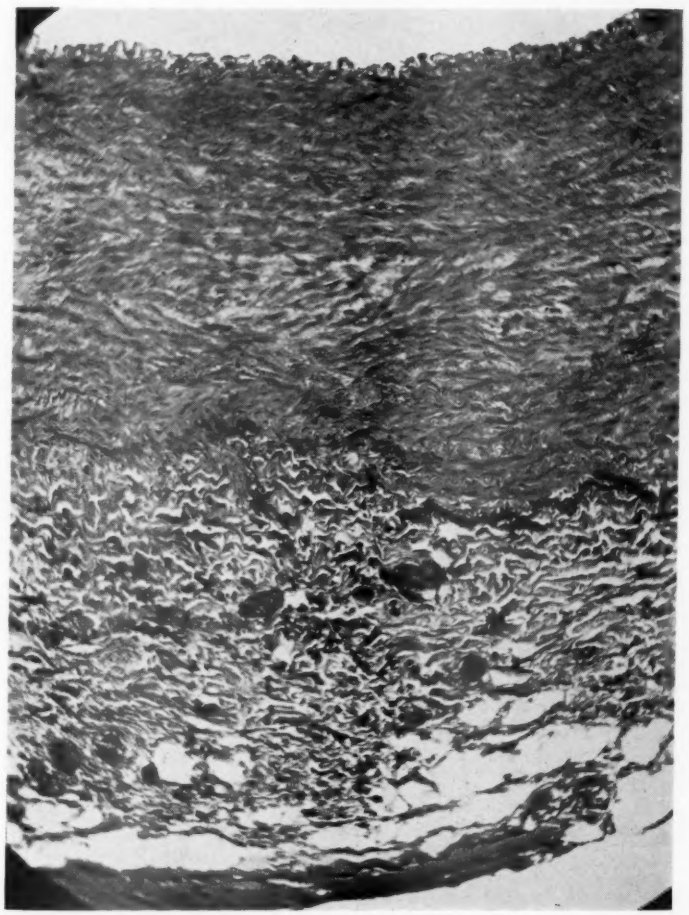

Fig. 5 *A*.—Photomicrograph of normal dog aorta (hematoxylin and eosin stain, ×100).

after a period of time the everted lips of the anastomosis have straightened out to present more nearly an end-to-end union. As a result of this slow adjustment at the site of anastomosis it is evident that certain of the sutures will come to lie beneath the endothelium as shown (Fig. 4, *A*, *B*, and *C*).

Microscopic Studies.—Histologic sections made of 16 normal aortas were compared with the 35 thawed frozen grafts after varying intervals of being maintained at either −27° C. or −70° C. Examination of 25 grafts stored at −27° C. for from 1 day to 8 months revealed that in contrast to the normal aortic tissue (Fig. 5, *A*) there are distinct degenerative changes appearing in

all layers within a few hours of the freezing process and progressing slowly during the period of storage.

After a few days of storage there is a disappearance of the endothelial and subendothelial cells, and those remaining present a pyknotic appearance. During the early periods of storage the internal elastic membrane and other elastic fibers appear relatively unchanged, although in some specimens there is a slight degree of vertical splitting of elastic fibers coupled with a patchy transverse fragmentation of the larger fibers.

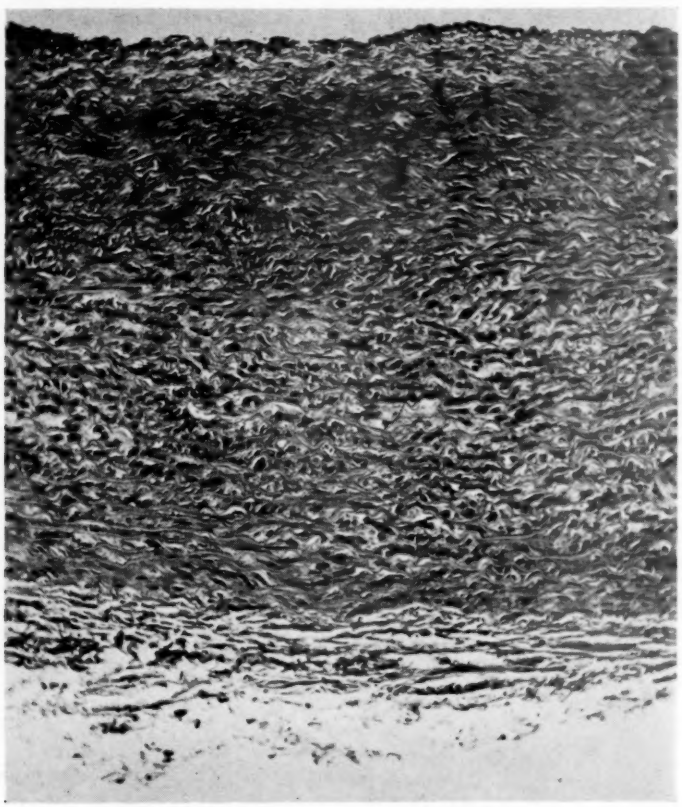

Fig. 5 *B*.—Microscopic section of dog aorta after storage for 3 days at -27° C. The endothelium is patchy and the smooth muscle cells have begun to degenerate. Formation of intercellular ice crystals produces the spaces in the media (hematoxlin and eosin stain, ×100).

The media microscopically is slightly thinner than that observed in the control sections. This change is partly the result of a progressive process of dehydration. The muscle cells contain much more darkly staining nuclei and finally disintegrate little by little, losing their individuality, and appearing as rather homogenous eosinophilic masses. After a few days there are definite clefts in the media which increase in time both as to number and size; these are thought to be the result of intercellular ice crystal formation. The adventitia alters in that the collagen fibers tend to swell and in some instances rupture, and there is a progressive loss of the capillaries and nerve fibers of this layer (Fig. 5, *B*).

Beyond 1 month of storage these changes have become much more definite with a disappearance of endothelial elements and a more definite change in the microscopic appearance of the elastic fibers, although generally the overall framework is maintained. The media becomes completely devoid of cellular detail and there are large clefts present. The collagen fibers of the adventitia are more consistently swollen than earlier (Fig. 5, *C*). These changes are less marked and develop more slowly during storage at 70° C.

Fig. 5 *C*.—Photomicrograph taken after 40 days' storage at -27° C. The loss of the endothelium and smooth muscle cells of the media has progressed, as has water loss. The many clefts and spaces in the media appear to be the result of ice crystallization (hematoxlin and eosin stain, ×100).

Examination of the graft following periods of implantation up to 90 days in the recipient dog reveals early changes. It has been quite difficult to demonstrate the spread of endothelium from the adjacent normal aorta by histologic methods, but by the end of 1 week there are definite patches of endothelial and subendothelial cells present on the surface of the inner elastic membrane. By the second week there is no question of the endothelization of the ends of the graft. These cells cross the line of anastomosis on the surface of the small thrombus or fibrin plug which generally fills in the cleft

produced by the everted edges. As this process continues, the graft eventually becomes completely lined by endothelium and a fibrocellular layer derived from the recipient aorta adjacent to each end of the graft. Consequently, the innermost layers of the graft in time are definitely thicker at each end than in the central portion. The inner elastic membrane in general has remained completely intact as has the meshwork of elastic fibers of the media, despite the degenerative changes already described. The media tends to become more compact and appears as a homogenous layer. Of the 26 grafts which had been implanted for periods up to 3 months, there has been a disposition of

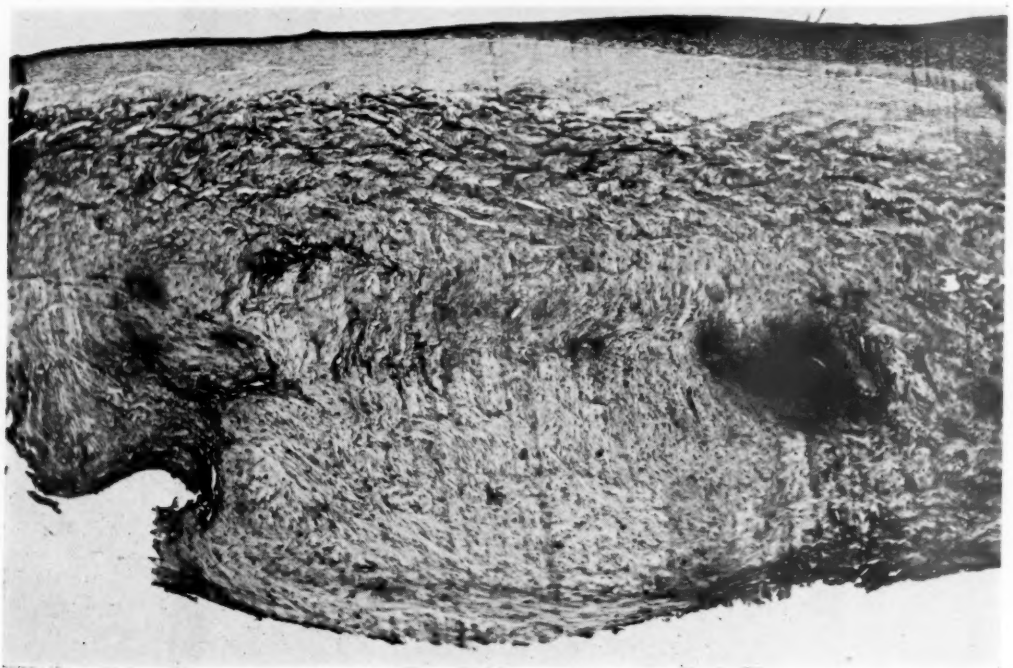

Fig. 6.—Photomicrograph of frozen graft which had been preserved at -27° C. for 30 days in a dog which had received no anticoagulation. Intimal layer is composed of a multilayered fibrocellular lining. Media is contracted with no normal smooth muscle cells remaining, but the elastic fibers are intact. Adventitia is greatly thickened due to marked increase of new fibrous tissue (hematoxylin and eosin stain, ×60).

calcium noted in only 1 instance, and this was in a graft removed after 58 days of implantation. It is anticipated, however, that our late studies may reveal such degeneration to be the rule rather than the exception. The adventitia appears to be the zone of greatest activity, with a marked round cell and polymorphonuclear response immediately following implantation. Within a matter of days there is an investment of the graft by a progressively thickening layer of fresh fibroblasts, which, however, have not yet been demonstrated to penetrate the media. After 10 days to 2 weeks, there can be observed capillaries and a tendency for the new fibrous tissue to be arranged in sheets or whorls. In these specimens studied up to 3 months after implantation there have not appeared to be any nerve fibers in this zone (Fig. 6).

Tissue Culture Studies.—Of 64 fresh aortic segments cultured, growth was excellent in all but 6, an incidence of 92 per cent (Fig. 7). In general, there has been a lag period of 3 to 4 days before this growth was observed, and the cells which proliferated appear to be mostly fibroblasts and in some instances endothelium. The specific details related to the characteristics of this growth will be described in a separate article. The few failures among the control group appeared in some instances to be either the result of bacterial contamination or from the use of serum which appeared to be unsatisfactory.

To date, none of the 27 frozen grafts, stored at either –27° C. or –70° C. and cultured after thawing at the time of implantation, has showed growth. In view of the histologic appearance of these grafts, we feel satisfied that they were indeed nonviable at the time of implantation.

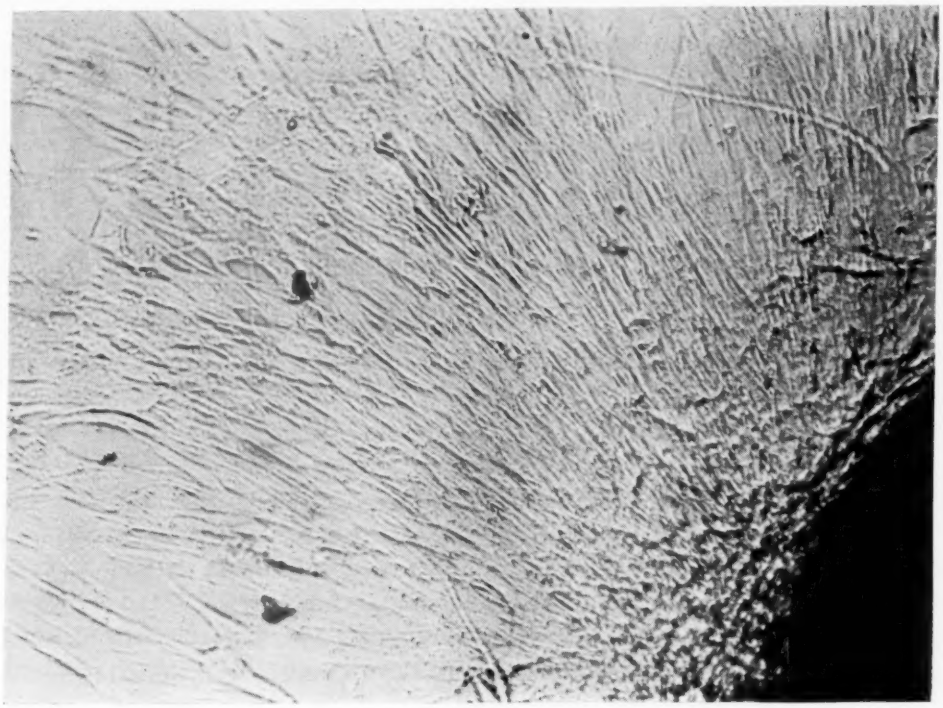

Fig. 7.—Photomicrograph of a 9 day living tissue culture of normal fresh abdominal aorta from an adult dog, showing an extensive outgrowth of cells from the explant (unstained, ×250).

After implantation of these grafts into recipient animals for 1 week or longer, 15 or 16 grafts so studied revealed excellent growth, or an incidence of 93 per cent. In all instances in which the proximal, middle, and distal thirds of the grafts were cultured separately, growth invariably appeared from the portions of the graft adjacent to normal aorta before it did in the middle third. It was quite interesting to note that there was an increase in the lag period before growth was observed; the volume of cellular growth was less than that of control tissue up to 2 weeks after implantation of the graft. Between the second and sixth week it was noted that there was a shorter lag period and that the amount of cellular growth revealed a more luxuriant and

apparently stimulated growth. After this period the amount of cellular growth appeared to be comparable to that observed in the control normal aorta (Fig. 8). There was noted as well a slight difference in the appearance of the cellular growth, with evidence of debris, many round cells, and small globules of fat. These findings are being studied further and will be reported at some later date.

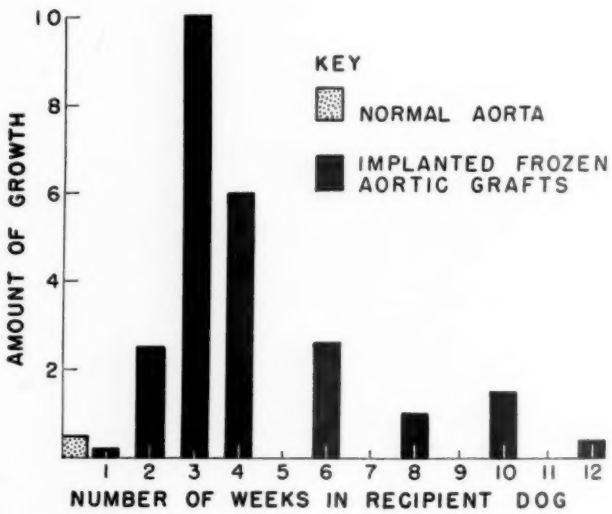

Fig. 8.—Chart showing relative amounts of cellular growth obtained by tissue culture from implanted frozen aortic grafts following their removal from recipient animal at varying periods of time.

DISCUSSION

Although varying degrees of success have been obtained with the use of various types of prostheses to bridge defects in arteries,[25-29] we have felt that the use of some form of animal tissue will prove to be most satisfactory in the final analysis. Although we have also been studying arterial and venous grafts preserved by various chemical means as well as by various types of nutrient media, our results to date, although short term admittedly, indicate that there is real promise in the frozen graft. To date we have been unable to determine any significant difference, at least functionally and from early microscopic examinations, resulting from our variations in treatment before quick freezing or in the process of thawing. It appears, however, that the degenerative changes observed in grafts stored at −27° C. are more severe and progressive than in grafts preserved at a much lower temperature.

From the work of DuBois and colleagues,[31] Hiner and co-workers,[32, 33] Luyet and Gehenio,[30] as well as other investigators interested in the refrigeration of animal tissues, we have learned that the rate of freezing, temperature and duration of frozen storage, and rate of thawing can be indeed of extreme importance in so far as maintenance of histologic architecture is concerned. To date, it would appear that our variations other than those of the conditions of storage have been too minor to produce an obvious effect. Nevertheless, we

do not feel that we have yet determined ideal standards for the freezing and storage of blood vessels. It has been shown that during freezing, storage, and thawing the pH of tissue is altered, which in turn affects the amount of swelling of tissue and protein denaturation.[34-38] The effects of freezing on the osmotic system and actual metabolism of tissues are also rather profound.[39-45]

While it is evident that the vascular surgeon is concerned primarily with the functional success and absence of late complications in the use of preserved vessel grafts, it is quite apparent that these basic factors so affected by freezing or refrigeration may be the keys to determining the best means of preserving a graft for clinical use. Luyet and Gehenio,[30] in their extensive review of the literature and original experiments, indicated that the most lethal and destructive zone involved in freezing tissues ranges from 0° C. to −40° C. It is in this zone that ice crystallization occurs, and freezing and storage within this zone is certain to be lethal if carried out beyond several hours. On the other hand, experiments in which extremely rapid freezing has been accomplished to temperatures well below −40° C., with rapid thawing, to escape as much as possible the lethal effects of the ice zone, have led, in some instances, to retention of vital functions.[16-30]

It is our intention to continue to explore the possibilities of further reducing degenerative changes by still more rapid freezing to much lower temperatures as by immersion in liquid air, but it must not be overlooked that such a technique would again run into some of the practical obstacles encountered in the refrigeration method. It has been our main purpose to find the simplest and yet most satisfactory method of preserving vessels for long periods of time for clinical use.

With the somewhat degenerated grafts obtained with storage at −27° C. there was a fair degree of success even without the use of anticoagulant drugs. The effect of these agents in permitting healing with satisfactory function appears to be rather significant and should be kept in mind when a graft is employed clinically in an area more likely to develop thrombosis than in the thoracic aorta. To our knowledge, this is the first time that anticoagulant drugs have been tried experimentally in conjunction with preserved vessel grafts. This was done since it was felt that in some instances these drugs would be used clinically. The results to date with the relatively small group of grafts preserved at below −60° C. show that they appear to function more satisfactorily than those preserved at a higher temperature, but only time will tell whether the long-term degenerative changes are less marked.

Although it has been felt desirable to demonstrate viability of the graft at time of implantation, since in the work done by Gross and associates the results with refrigerated grafts were better than those with the quick-frozen type,[16-17] it was demonstrated several decades ago that viability is indeed not a necessary prerequisite for a functioning graft. Indeed, 1 graft preserved in formaldehyde was demonstrated to be perfectly functioning and patent 11 years following implantation.[14] It might be well to point out a few factors which throw doubt on the fact that it is the use during the period of viability

per se which has accounted for the difference in success in the previous studies. It has been demonstrated by histologic methods that after a few weeks in a nutrient medium a graft begins to shed the endothelium, and after implantation may reveal no endothelium in as early as 24 hours.[46] In addition, workers in the field of tissue culture are well aware of the difficulties in obtaining cultures of endothelial cells and particularly smooth muscle cells. It has appeared that the growth which has been demonstrated in the segments preserved in a nutrient medium is, after all, primarily fibroblasts derived from the adventitial layers, and it is further a fact that the percentage of success in growing even these tissues beyond a few weeks drops off perceptibly. By our technique, which makes use of only the innermost portions of the graft, we have been unable to demonstrate cellular growth from segments preserved in nutrient medium beyond 23 days, and we are now studying segments planted as full-thickness colonies to determine whether this factor explains the difference with the results of Gross and co-workers. In any event, one must assume that many of the grafts preserved by this method have viability restricted to only a few fibroblasts, and it has been suggested that the viability of these cells in the adventitia is not retained after implantation.[46] Furthermore, recent work indicates that even though a definite degeneration occurs in grafts preserved in the nutrient medium beyond 40 days, a high degree of functional success was obtainable with those that are presumably completely dead.[46] Similar experiments in our own laboratory have confirmed this fact.

From a basis of animal experimentation, our results with the worst set of frozen grafts, that is, those preserved or stored at −27° C. and used without any anticoagulant drugs, were much better than those observed with frozen grafts by Gross and his associates, and only slightly worse than the results of their series employing grafts preserved in a nutrient medium. Indeed, our results to date with the grafts stored at below −60° C. coupled with the use of anticoagulant drugs are fully as satisfactory as the results with grafts in the animals studied by Gross and associates,[16, 17] and Swan and colleagues[46] (Table I).

If it continues to be difficult to obtain grafts even in large cities, we may be faced with the need for accepting the use of some form of frozen grafts clinically, at least to supplement a store maintained by the refrigeration method. We are continuing our exploration of various types of freezing and other means of preservation with the hope that we or others in the field may find a completely satisfactory substitute.

SUMMARY

1. Quick freezing at −72° C. and storage at very low temperatures appear to be satisfactory means of preserving aortic homografts.

2. The freezing and thawing process we have employed with aortic segments of dogs appears to destroy the viability of the graft, as indicated by histologic and tissue culture methods.

3. Experimentally we have had success with the use of the frozen aortic homograft implanted for from 2 days to 10 months. A sizeable group of animals is being maintained for long-term study.

4. Anticoagulant drugs were employed with some grafts with an improved percentage of function.

5. The frozen homologous aortic graft appears to act as a framework onto which viable cellular elements of the recipient aorta grow, as demonstrated by tissue culture and histologic sections after 1 week following implantation. Certain characteristics of this new growth have been noted as differing from normal by the tissue culture method and are being studied further.

6. Further experiments are being carried out studying additional variations of the freezing method as well as those of preservation by chemical means and nutrient media.

We wish to acknowledge the assistance of Miss Borrelli and Miss Samuels of the Surgical Chemistry Laboratory in performing the determinations of the prothrombin time. We wish to thank Miss D. Mapes and her assistants for their help during operation and in the postoperative care of the animals.

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A METHOD OF PRODUCING COARCTATION OF THE AORTA IN THE GROWING ANIMAL

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IT IS well established that complete and permanent acute occlusion of the aortic arch cannot be accomplished in the experimental animal without paralysis of the hindquarters or death. If the stenosis is gradual, allowing time for the development of an adequate collateral blood supply, the occlusion may be made complete without serious impairment to life or limb.

Early investigations on methods of obliterating the aortic lumen were directed toward the treatment of aneurysms and traumatic lesions. To this end, a variety of clamps, tapes, fascial plugs, and irritation substances have been used with some success.[1-9] Those methods which were based upon external compression frequently caused necrosis of the aortic wall and fatal hemorrhage.

Quite apart from the therapeutic need, a satisfactory technique for producing partial and complete aortic arch occlusion is desirable, for it furnishes a method of studying certain problems in circulatory physiology.[10-19] It is possible, with mechanical devices, to create a partial aortic occlusion.[17] However, such methods have the disadvantage of requiring the use of adult animals, and, furthermore, the stenosis is created acutely. It would be preferable, and more like human coarctation, for the lesion to exist from birth, or soon thereafter, so that the influence of the coarctation could be exerted during the growth and development of the animal.

We have been using a simple technique which meets this requirement.[20-21] It consists of loosely tying a braided silk ligature about the aortic arch of a newborn animal without narrowing the lumen (Fig. 1). As the puppy grows, the ligature remains in place, causing a narrowing which becomes relatively greater as the aorta increases in size (Figs. 2 and 3). At the same time, an extensive collateral blood supply develops around the area of constriction, which subsequently permits the complete occlusion of the thoracic aorta without causing paralysis or death. In none of the animals has hemorrhage occurred, nor has the ligature eroded through the intima. Holman used this technique to narrow the intrapericardial portions of the aorta and pulmonary conus in order that he might study cardiac hypertrophy, and he, likewise, found that hemorrhage did not occur.[20]

METHOD

Two litters of puppies were used in the experiments. In Litter A the animals were operated upon 48 hours after birth. In Litter B the animals were 14 days old. Light anesthesia was established with ether. A small intratracheal tube was inserted, and the lungs were rhythmically expanded by mouth while

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the thoracotomy was performed. Under aseptic precautions, a short intercostal incision was made in the left thorax. The aorta just beyond the left subclavian artery was freed with a small, curved hemostat, and a No. 1 braided silk ligature was loosely tied around it. Care was taken not to constrict the lumen. The lung was inflated, and the thorax was closed with interrupted silk sutures. Of 4 puppies in Litter A, 2 survived the operation and lived to be adult dogs. Of 5 puppies in Litter B, 3 were operated upon and survived, 2 were kept as controls, and all lived to be full-grown dogs. Observations on these animals were conducted over a period of from 12 to 50 months.

Fig. 1.—Showing the placement of the ligature in the newborn puppy.

Intra-arterial pressures were optically recorded by a sensitive Hamilton manometer connected to Cournand needles which were placed in the femoral and brachial arteries through small skin incisions. A simultaneous electrocardiogram was taken. Second observations were made in 4 animals, the time interval between observations being as indicated in Fig. 4. Systolic and diastolic pressures were measured through several respiratory cycles and averaged. Mean

pressures were computed by planimetric integration of the area under the pressure curves. Calculations were made of the time interval elapsing from the beginning of the QRS complex of the electrocardiogram to the start of the systolic rise of the arterial pulse wave (QFA_s), as well as to the peak of the arterial

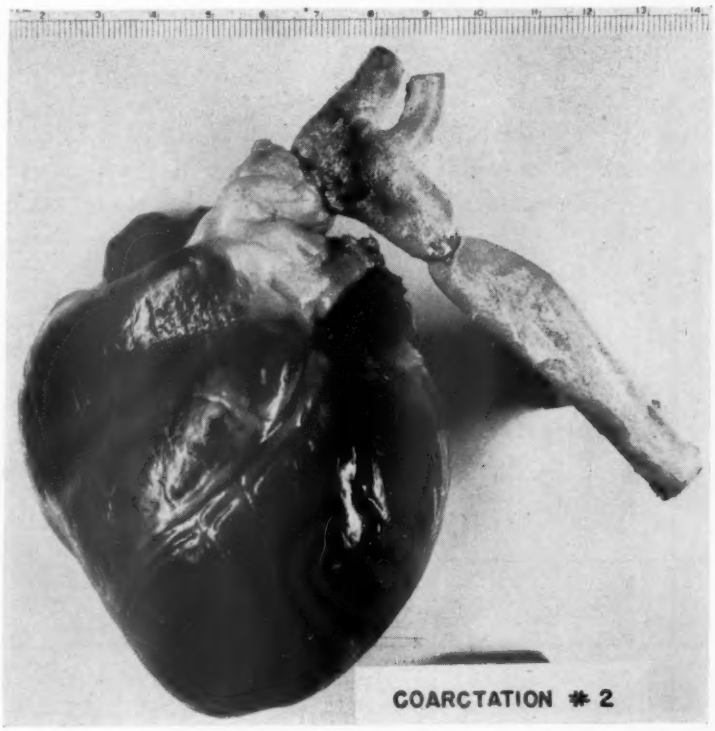

Fig. 2.—Appearance of the heart and aorta when the animal (B2) was 14 months old. Note the enlargement of the left ventricle and the dilatation of the aorta distal to the stenosis.

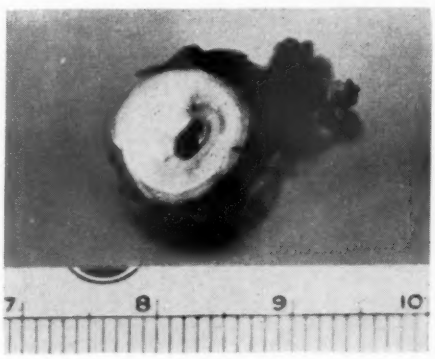

Fig. 3.—Appearance of the area of stenosis when the animal was approximately 1 year old.

pulse wave, (QFA_{ps}). At least 10 determinations were made in each animal, and the results averaged (Table I). During the blood pressure determinations, the animals were lightly anesthetized with intravenous veterinary Nembutal, with no significant circulatory depression resulting. Heart rates varied from

TABLE I. SUMMARY OF INTRA-ARTERIAL BLOOD PRESSURE MEASUREMENTS (M.M. HG.) IN CONTROL ANIMALS AND EXPERIMENTAL ANIMALS WITH COARCTATION OF THE AORTA

ANIMAL NUMBER	ARTERY	SYSTOLIC PRESSURE	DIASTOLIC PRESSURE	MEAN PRESSURE	PULSE PRESSURE	DATE OF MEASUREMENT	REMARKS
Litter A							Aorta completely tied off 1-10-50
1	Brachial	243	178	204	65		
	Femoral	165	140	151	25	6-12-50	
Litter B							
1	Brachial	176	126	151	50		
	Femoral	136	114	124	22	10-6-49	
1	Brachial	157	106	126	51		
	Femoral	118	99	109	19	2-2-50	Sacrificed 2-2-50
2	Brachial	182	136	154	46		
	Femoral	151	124	138	27	10-4-49 A.M.	Aorta completely tied off 10-4-49 P.M.
2	Brachial	192	141	161	51		
	Femoral	112	104	108	8	10-27-49	
2	Brachial	171	129	144	42		
	Femoral	117	106	109	11	1-5-50	Sacrificed 1-9-50
3	Brachial	160	111	136	49		
	Femoral	138	116	125	22	9-13-49	
3	Brachial	227	174	198	53		Aorta completely tied off 9-27-49
	Femoral	154	141	149	13	10-24-49	
3	Brachial	181	136	158	45		Coarctation repaired 12-3-49
	Femoral	170	116	135	54	12-20-49	Sacrificed 6-15-50
4	Brachial	158	108	132	50		
(Control)	Femoral	155	104	131	51	9-20-49	
4	Brachial	148	114	130	34		
(Control)	Femoral	165	112	133	53	5-4-50	Sacrificed 6-15-50
5	Brachial	138	102	118	36		
(Control)	Femoral	132	96	110	36	8-11-49	
5	Brachial	142	112	128	30		
	Femoral	157	112	132	45	1-21-50	Died 2-20-50

170 to 214 per minute. Electrocardiograms were normal. Arterial oxygen saturations, analyzed on the several animals on 10 occasions, varied from 85 per cent to 95 per cent.

Both the body weight and the fresh heart weight were recorded at death, after which the hearts were fixed in 10 per cent formalin. Separate weights of the fixed ventricles were determined* by the following technique: the atria, valves, and epicardial fat were carefully dissected from the ventricles at the atrioventricular groove and discarded. The right ventricle was removed by sharp dissection, and the interventricular septum, adjacent to the right ventricle, was separated from the left ventricle. The 3 parts of muscle mass were individually weighed. One-half of the weight of the interventricular septum was added to the weight of each ventricle.

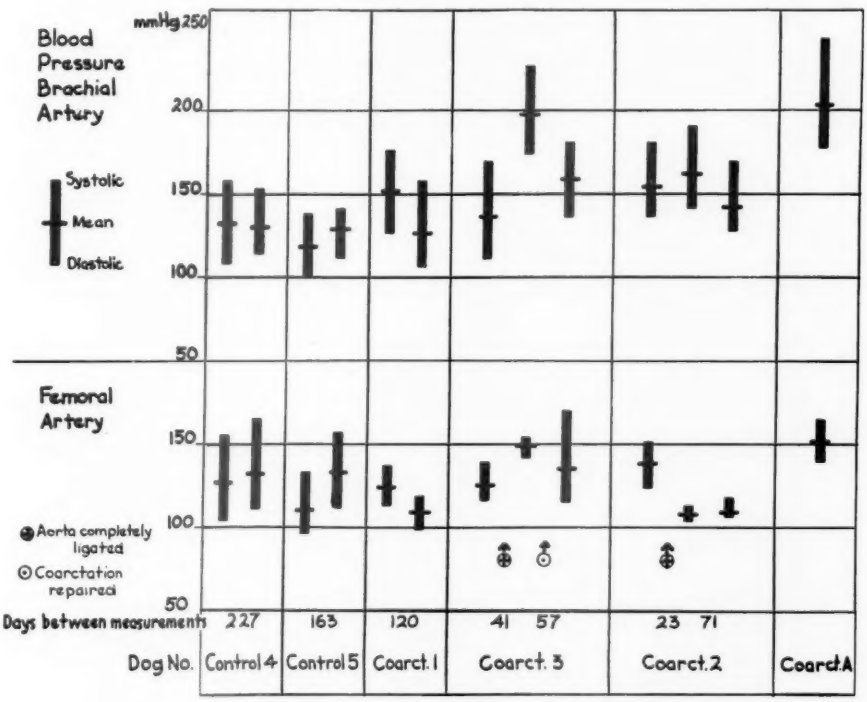

Fig. 4.—Composite chart showing the blood pressure determinations on the experimental animals.

Effect of the Coarctation on the Intra-Arterial Blood Pressure.—Partial constriction of the aorta to a lumen of about 2 mm., caused by its growth over the ligature, resulted in a definite increase in systolic and diastolic pressure in the upper extremities in 1 animal (Coarct. 2) as compared with the controls. The rise was approximately 36 mm. in systolic and 25 mm. in diastolic pressure. A slight rise was present in the other 2 animals. A more consistent difference was present in the femoral arterial pulse pressures, averaging 24 mm., or about 50 per cent lower than the average of measurements in the control animals (Fig. 4). In each animal this was associated with an alteration in the contour of the

*By Dr. J. S. Cheredes, Department of Pathology.

femoral pulse, which resembled that obtained from human cases of moderate degrees of coarctation. However, there was no detectable prolongation of the QFA_s and QFA_{ps} intervals compared to the same intervals in control animals. Mean pressures in the femoral artery were similar to those in control animals (Table I).

It was interesting to observe the effect of complete ligation of the aorta in the animals which had had a previous partial constriction. Two of these developed a distinct hypertension, 227/174 and 243/178 mm. Hg, in the brachial artery (B3 and A1), and a slight further rise occurred in the other (B2). In

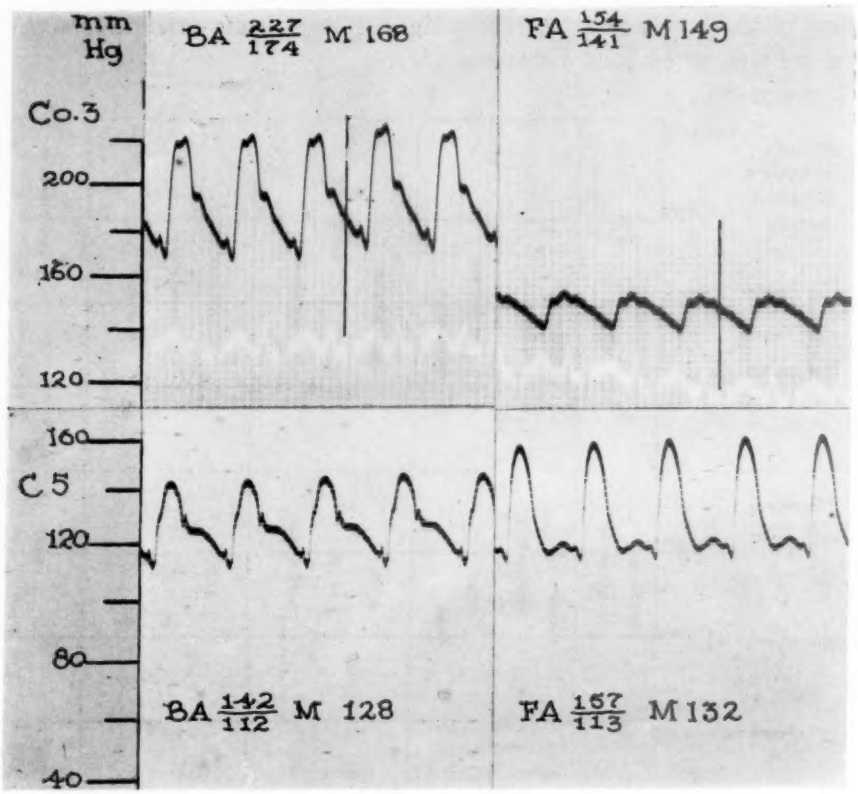

Fig. 5.—Arterial tracings made from brachial and femoral arteries of dog with experimental coarctation (above) and a normal control animal (below). The vertical lines in the upper tracings mark the beginning of the QRS complex of the simultaneous electrocardiogram. Fine vertical lines are 0.04 second apart.

2 animals (B2 and B3) a striking decrease in the femoral arterial pulse pressure to values of 8 and 13 mm. Hg occurred. Arterial tracings made from these animals resembled those obtained from human cases with a severe degree of coarctation (Fig. 5). Compared with control animals, the QFA_s time was prolonged an average of 0.025, and the QFA_{ps} time 0.04 second. The decrease in femoral arterial pulse pressure in A1 was not so striking, and no delay in the arterial pulse could be detected, although the aorta was completely occluded. The mean femoral arterial pressure rose in 1 animal and fell in another after complete ligation.

After excision of the area of coarctation in 1 animal (B3) and end-to-end anastomosis of the aorta, systolic and diastolic pressures fell in the upper extremity, and the pulse pressure in the lower extremity increased to a normal value with a decrease in the mean pressure. The contour of the femoral pulse resembled that of the control animals.

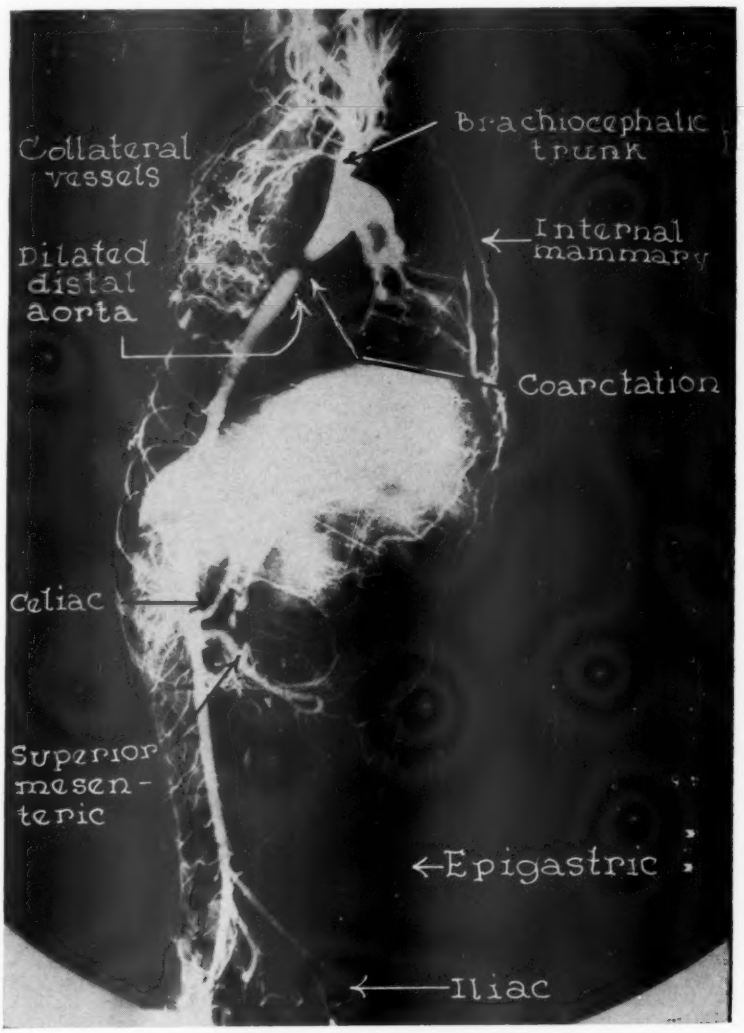

Fig. 6 (Experiment A1).—Injection of arterial system with Hill's mixture. Note the complete coarctation and the extensive collateral circulation.

Anatomic Effect of the Ligature.—There was an obvious enlargement of the left ventricle in the animals which had experimental coarctation, and this relative increase in size was shown to be due to hypertrophy (Table II). The ligature had remained in place in each instance, causing a narrowing of the aortic lumen to a diameter of about 2 mm. The aorta distal to the stenosis was larger than that proximal, and this difference in size persisted after complete ligation. An abundant collateral blood supply developed around the experimental coarctation (Fig. 6). Microscopic studies of the area of stenosis revealed that the

ligature had cut through the adventitia, and lay in the media (Fig. 7). Healing had taken place behind it so that the outermost parts of the media and adventitia were united by fibrous tissue. The intima was intact. When an additional ligature was tied firmly beyond the original one, the tissue beneath it had the microscopic appearance of having been killed by pressure. No rupture or

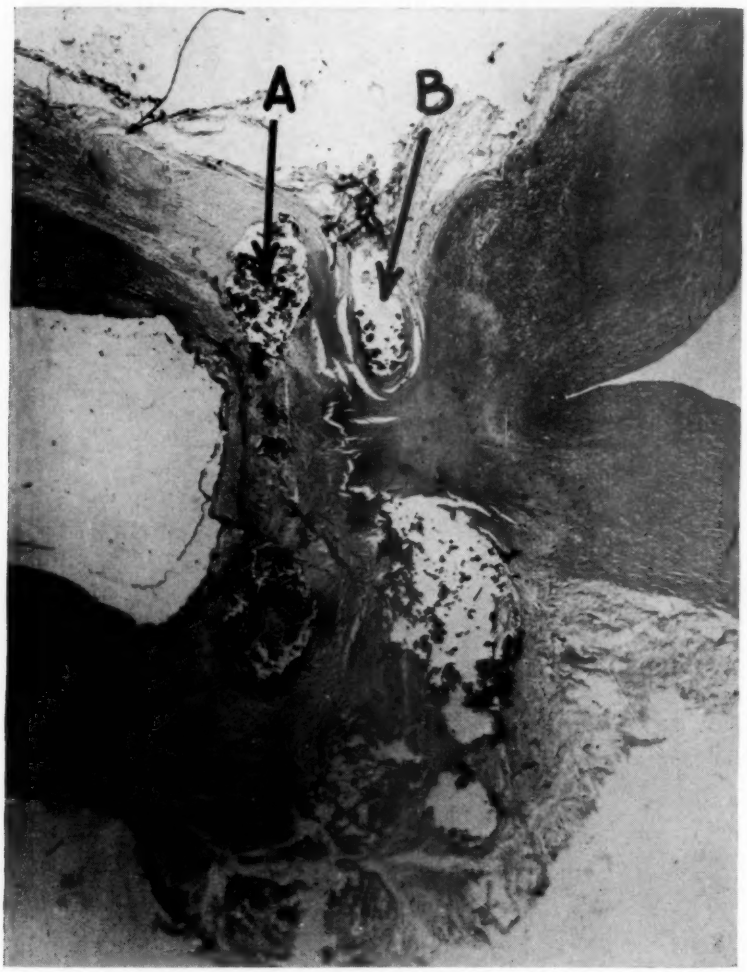

Fig. 7.—Longitudinal section through the area of coarctation about 1 mm. from the center of the previous lumen. Note that the original ligature, *A*, lies within the aortic wall, and that the intima is intact. The second ligature, *B*, was tied firmly just beyond the original one 3 months before the animal was sacrificed. It caused pressure necrosis of the aortic wall beneath it, but rupture did not occur.

hemorrhage occurred, probably because there was sufficient fibrous tissue around the initial ligature to protect the aorta. Furthermore, the weakened area caused by the second ligature was exposed to the greatly reduced pulse pressure in the distal aortic segment. Although ligation of the aorta was used to complete the occlusion, it was felt that division beyond the initial ligature, with suture of the ends, would be feasible.

TABLE II. A COMPARISON OF HEART AND BODY WEIGHTS IN CONTROL AND EXPERIMENTAL ANIMALS

ANIMAL NUMBER, LITTER B	ANIMAL WEIGHT (KG.)	HEART WEIGHT (GM.*)	LEFT VENTRICLE (GM.†)	RIGHT VENTRICLE (GM.†)	LEFT/RIGHT VENTRICULAR RATIO
1	22.0	212	89	45	1.98
2	23.0	220	108	40	2.70
3	22.9	210	106	52	2.12
4 (Control)	16.2	145	71	41	1.73
5 (Control)	19.5	160	65	39	1.66

*Fresh tissue.
†Fixed tissue.

PROTOCOLS

EXPERIMENT A1.—The experiment was done on a 48-hour-old female dog, terrier type, on April 2, 1946. Under light ether anesthesia the left thorax was entered through an intercostal incision. The aorta was identified and encircled 6 mm. beyond the left subclavian artery with a No. 1 braided silk ligature, loosely tied with a square knot. After the wound had been closed with interrupted silk, the puppy was returned to its mother.

During the course of the following year, a soft systolic murmur became audible along the posterior left thorax, and the femoral pulses felt weaker than the brachial pulses. On Jan. 10, 1950, a thoracotomy showed that the aorta proximal to the ligature had a maximum diameter of 12 mm., just outside the ligature it was 7 mm., while distal to the ligature it measured 14 mm. A slight systolic thrill, perceptible in the aorta beyond the constriction, could be obliterated by pressure upon the area of stenosis. The aorta was then tied very firmly with another No. 1 braided silk ligature at a point slightly beyond the original one, following which the thorax was closed. Intra-arterial blood pressure measurements taken on June 16, 1950, showed a brachial pressure of 243/178 mm. Hg, and a femoral pressure of 165/140 mm. Hg. A blood urea on that same day was found to be 28 mg. per cent. This animal successfully delivered 4 litters of puppies. Examination of the eye grounds showed no retinal hemorrhages. On Sept. 1, 1950, the animal died suddenly of an intussusception. The arteries, injected with Hill's mixture, showed an extensive collateral circulation (Fig. 6) and complete coarctation. The body weight was 7 kg. The heart weighed 88 Gm., and showed marked hypertrophy of the left ventricle.

EXPERIMENT A2.—The experiment was done on a 48-hour-old male dog, terrier type, on April 2, 1946. Under light ether anesthesia the left thorax was entered through an intercostal incision. The aorta was loosely encircled with a No. 1 braided silk ligature, placed, in this instance, about 2 cm. beyond the left subclavian artery. The thorax was closed with interrupted silk. In a few months a soft systolic murmur developed along the posterior left thorax. At the same time, the femoral pulses became weaker than the brachial. On April 2, 1947, the animal was inadvertently killed during an angiocardiographic study. The arterial system was subsequently studied with Hill's bismuth mixture, roentgenograms revealing that an extensive collateral blood supply had developed about the area of contriction. At necropsy, a 2 mm. lumen was found at the site of constriction. The aorta distal to the constriction was larger than that proximal to it.

Hound Puppies, 14 days old, November 30, 1948.

In Experiments B1, B2, and B3, the procedure was identical, consisting of loosely tying a No. 1 braided silk ligature around the aorta about 6 mm. beyond the left subclavian artery.

EXPERIMENT B1.—The experiment was done Nov. 30, 1948, on a 14-day-old female hound puppy. At no time during life could one hear a definite systolic murmur. Intra-arterial pressure measurements on Oct. 6, 1949, revealed a brachial pressure of 176/126, and a femoral

pressure of 136/114. On this day the blood urea was 18 mg. per cent. On Feb. 2, 1950, the animal, which then weighed 22 kg., was sacrificed. The heart weighed 212 Gm. Bougie measurements revealed that proximal to the constriction the aorta admitted a No. 34, at the area of constriction, a No. 12, and distal to the constriction, a No. 40. The left ventricle, when fixed, weighed 89 Gm.. and the right, 45 Gm.

EXPERIMENT B2.—The experiment was done Nov. 30, 1948, on a 14-day-old female hound puppy. Within several months the animal developed a soft systolic murmur toward the posterior left thorax, and the femoral pulses seemed weaker than the brachial. On Sept. 29, 1949, the left thorax was opened through the fourth intercostal space. Increased vascularity of the thoracic wall due to the extensive collateral circulation was obvious, and the intercostal arteries were enlarged. Further inspection revealed that a marked constriction of the aorta had developed at the site of the ligature. The aorta proximal to the stenosis measured 15 mm., at the ligature, 5 mm., and distal to the constriction, 20 mm. It was apparent that a slight thrill, perceptible distal to the stenosis, could be obliterated by pressure on the stricture. The aorta was then firmly tied a few mm. beyond the previous ligature with No. 1 braided silk, and the wound was closed. The animal showed no ill effects from complete occlusion of the aorta. Intra-arterial blood pressure measurements, taken before and after total closure of the aorta, are recorded in Table I. On Oct. 4, 1949, the blood urea was 18 mg. per cent, and on Oct. 27, 1949, it was 27 mg. per cent. On Jan. 9, 1950, the animal, weighing 23.00 kg., was sacrificed. Injection of the arterial tree with Hill's mixture revealed an extensive collateral blood supply. The heart weighed 220 Gm. There was no lumen at the site of constriction. The aorta distal to the coarctation was larger than proximal to it (Fig. 2). The fixed left ventricle weighed 108 Gm., the right 40 Gm.

EXPERIMENT B3.—The experiment was done Nov. 30, 1948, on a 14-day-old male hound puppy. On Sept. 27, 1949, when the left thorax was opened through the fifth intercostal space a great many dilated vessels with blood under tension were encountered in the thoracic wall. At that time, the aorta proximal to the stenosis measured 12 mm., and beyond it, 19 mm. A moderate thrill could be felt just distal to the constriction. Two No. 1 braided silk ligatures were tied firmly about the aorta just distal to the area of coarctation, stopping the thrill, and the wound was closed. The animal showed no ill effects from the ligation. Intra-arterial blood pressure determinations before total ligation mainly showed that the pulse pressure in the brachial artery was about twice that in the femoral artery. After complete ligation, the pressure rose rather markedly, and the pulse pressure in that brachial artery was approximately 4 times that in the femoral (Fig. 5). On Dec. 3, 1949, the stenotic area was excised, and the aortic lumen was restored by end-to-end suture. No lumen was found in the resected specimen. Blood pressure determinations subsequently showed a drop in mean pressures, but some degree of hypertension persisted. After repair, the femoral pulse pressure was higher than the brachial. The animal was sacrificed on June 15, 1950. Inspection of the site of repair revealed a smooth intimal surface throughout, with a uniform lumen.

EXPERIMENT B4 (CONTROL).—This female dog was kept in the same kennel with its litter mates. Intra-arterial blood pressure determinations were made on 2 occasions (Fig. 4). On June 16, 1950, the animal, weighing 16.2 kg., was sacrificed. The fresh heart weighed 145 Gm. the left ventricle, 65 Gm., and the right ventricle, 39 Gm.

EXPERIMENT B5 (CONTROL).—This female dog was kept in the same kennel with its litter mates for the first 6 months. It was apparent that it was being attacked quite frequently by the other dogs, and on several occasions it had to be placed in a single cage to recover from bites. On Feb. 20, 1950, it died rather suddenly. Necropsy revealed that it had a generalized peritonitis, caused by a ruptured gastric ulcer. The body weight totalled 19.5 kg., the fresh heart, 160 Gm., the fixed left ventricle, 65 Gm., and the right ventricle, 39 Gm. A blood urea analysis on Oct. 10, 1949, was 23 mg. per cent.

SUMMARY

A method of producing partial and complete coarctation of the thoracic aorta in the growing animal is described. A rich collateral blood supply de-

veloped. Brachial and femoral intra-arterial blood pressure determinations indicated that chronic partial constriction of the aorta caused a distinct fall in femoral pulse pressure and a slight rise in the brachial arterial pressure. Complete occlusion of the aorta produced distinct arterial hypertension in the upper extremities, with a marked fall in femoral arterial pulse pressure, and a characteristic delay and deformation of the pulse curve. The principle of gradual occlusion of a great vessel by its growth over a ligature might be applied to other vessels in the study of circulatory physiology.

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CARDIAC MASSAGE IN OPERATING ROOM DEATHS

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ONCE a hopeless tragedy, sudden cardiac arrest may now be effectively treated by the efficient and skillful cooperation of the surgeon and anesthetist. The heart, as well as the entire body, retains for some time its potentiality to be revived.

Oxygen deprivation results in permanent damage, first, to the nervous system. It has been demonstrated that the cells of the cerebral cortex are most sensitive to anoxia. Permanent changes in psychic behavior have been observed after a 3 minute, 20 second interruption of the circulation, with complete dementia, blindness, and other changes after 7 minutes and 36 seconds. While cardiac rhythm can be re-established over 8 minutes after circulatory interruption, damage is so extensive that the patient will die in a few hours to 2 or 3 days without regaining consciousness.

The maximum time allowable between the onset of circulatory arrest and the start of effective treatment to attain complete recovery has been variously reported as 3 to 8 minutes, but it is generally recognized that 5 minutes is the upper limit of safety. A shorter time limit may be expected if the cardiac arrest occurs in the presence of a pre-existing hypoxia, as is often the case. Cardiac massage combined with artificial respiration can maintain an adequate circulation of oxygenated blood to protect the nervous system from permanent damage for a considerable time.

In the absence of known heart disease, fatal cardiac arrest occurs under various circumstances. Of interest to us is sudden death occurring during induction of anesthesia, at surgery, or in the delivery room, whether due to the anethesia, the operative procedure, or to the administration of certain drugs. Cardiac arrest in the operating room affords the best opportunity for prompt effective treatment.

A survey by Trent in 1944 covering a 12 year period and 39,880 general or spinal anesthetics, discovered 38 operating room deaths, of which 27 (.677 per 1000) were related to the anesthetic. Dillon reported 46 operating room deaths in 28,000 anesthetics administered by trained anesthetists during the period of July 1, 1946, to April 1, 1948, in a general hospital. Six out of these 46 deaths were due to cardiac arrest. The incidence in smaller hospitals where expert anesthetists are not available is undoubtedly proportionately higher.

The heart's rhythm is constantly influenced by nervous, hormonal, and chemical stimuli, and its irritability or response to these stimuli is modified by the state of the heart's nutrition and its blood and oxygen supply. Physiologic

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stimuli either accelerate or retard the heart through its pacemaker, and normally overaction is guarded against by a delicate cardioregulatory buffer system. If, however, the irritability of the myocardium is much increased, or the cardioregulatory reflexes become hyperactive, arrhythmias and tachycardia leading to fibrillation or to bradycardia and asystole can occur.

These two conditions, ventricular fibrillation and cardiac standstill, are the two chief causes of sudden cardiac arrest. They differ fundamentally in mechanism and also in their treatment. Unfortunately, it is not always possible to predict from the circumstances or symptoms the type with which one is dealing, but, generally speaking, sudden death occurring during light anesthesia and excitement is usually due to ventricular fibrillation. Cardiac standstill more commonly follows deep anesthesia or prolonged anoxia.

Regardless of the type of cardiac arrest, the etiological factors are all related either to the myocardium or to the cardioregulatory mechanism. The surgical patient may come to operation with the myocardium hyperirritable from bacterial or other toxins in the circulation, chemical imbalance, or from areas of ischemia from coronary disease. Hypoglycemia may also increase myocardial irritability. Worry or fear induces oversecretion of epinephrine. So-called "thymic deaths" are probably due to cardiac arrest from hypersensitive cardioregulatory reflexes. Hypersensitivity to certain drugs may result in near-fatal to fatal overaction. This has been reported with pituitrin, anesthetic agents, mercurial diuretics, and so on.

Clinically, more than one cause may contribute to cardiac arrest. The most important causes are herewith considered separately.

Oxygen Deficiency.—Low oxygen levels in the blood stimulate the carotid sinus and the cardio-inhibitory reflexes. Low oxygen and high carbon dioxide each cause oversecretion of epinephrine. Hypoxia furthermore sensitizes the myocardium to epinephrine. Thus we have factors favoring either fibrillation or standstill. Beck and Mautz indicated that general lack of oxygen usually causes cardiac standstill, while focal hypoxia in the myocardium favors fibrillation. During surgery, lack of oxygen may result from obstructed air passages, depression of the respiration by premedication or too deep anesthesia, and by a fall in blood pressure. Surgery on the face and dark skin makes it difficult to recognize cyanosis.

Anesthesia.—Anesthetics may cause death by direct toxic action on the heart or by too deep anesthesia in which respiration is first paralyzed, followed by heart failure. In the early history of anesthesia, chloroform was a frequent cause of cardiac arrest. Its effect is due to its toxic action. Cyclopropane sensitizes the heart to epinephrine and has a strong parasympathetic or depressing action on the heart. The excitement stage of any anesthetic accompanied by fear and overactive reflexes is always more hazardous.

Spinal anesthesia, especially in smaller hospitals, is not uncommonly associated with operating room deaths. Veal and Van Werden in 1936 reported 30 immediate fatalities in 33,811 spinal anesthetics. The usual mechanism is

tissue hypoxia, especially of the myocardium, due to depression of the blood pressure. The coronary circulation flows largely during diastole and low diastolic pressure seriously impairs the heart's blood supply.

Reflex Stimuli.—Under light anesthesia nerve reflexes affecting the heart are hyperactive and readily cause arrhythmias, but especially when the myocardium is made more sensitive by cyclopropane, epinephrine, Pituitrin, hypoxia, bacterial toxins, and so on. The vagovagal reflex is most important in chest and abdominal surgery where handling of viscera under light anesthesia may cause arrhythmia and cardiac arrest. "Pleural shock" and death have occurred at the time of introduction of a thoracentesis needle.

Drugs Contributing to Cardiac Arrest.—Barbiturates given intravenously exhibit a parasympathetic effect on the heart. They also sensitize the heart to epinephrine and Pituitrin. Epinephrine, while increasing coronary flow, also increases the heart's work and sensitizes the heart to cyclopropane. Ephedrine may likewise increase myocardial irritability, while Neosynephrine does not. Fatal reactions have occurred from the accidental or intentional use of Pituitrin intravenously. Since Pituitrin is a powerful coronary constrictor, it may cause sufficient myocardial ischemia and dilatation to result in cardiac standstill. Ventricular fibrillation may follow the use of Pituitrin, especially if the myocardium is sensitized by any of the aforementioned factors.

Prophylaxis.—Most cases of cardiac stoppage and fibrillation can be prevented by careful attention to the following precautions:

1. Insurance of adequate oxygenation by use of airways, oxygen, and so on; artificial respiration should be instituted immediately when there is respiratory paralysis from spinal anesthesia or by overaction of curare
2. Maintenance of blood pressure
3. Avoidance of profound anesthesia
4. Avoidance of premature intubation, especially under cyclopropane anesthesia
5. Use of topical or local anesthetics to diminish reflex irritability as may be seen during tracheal intubation and thoracentesis
6. Reduction of cardiac irritability by the epicardial and systemic administration of drugs as a protection in thoracic surgery; the use of procaine intravenously or its actual injection in the pericardial cavity has been recommended
7. Cautious use of a combination of drugs which sensitize the myocardium, as in the use of epinephrine and cyclopropane, and Pituitrin, cyclopropane, and ephedrine
8. Proper and adequate preanesthetic preparation with antibiotics, correction of chemical imbalance, sedation, antispasmodics, autonomic drugs, and even the use of quinidine in cases where auricular or ventricular fibrillation may be anticipated during the operative or postoperative period.

The type of management of cardiac arrests depends upon whether or not it is due to fibrillation or standstill. In either case, the first essential is team-

work. Here the anesthetist, who has followed the patient's condition and is familiar with the effects of the drugs and anesthetics used, is in a position to recognize the probable type of cardiac arrest. Once cardiac arrest has been diagnosed there should be no delay in instituting active treatment. Bailey recommended the appointment of a timekeeper, a student or a nurse, who keeps the surgeon informed of the exact time which has elapsed since the anesthetist sounded the warning of cardiac stoppage. A tray with necessary supplies should always be ready. This should contain syringes, 2 c.c, 5 c.c, and 10 c.c; needles, 20 to 22 gauge, 3 inches to 4 inches, 20 gauge to 1½ inches; capsule of Coramine and amyl nitrite; drugs and solution, 2 per cent Novocain, epinephrine, and Cedilanid.

The main objectives in the treatment of cardiac arrest are: (1) ventilation of the lungs with oxygen, and (2) restoration of cardiac action.

Oxygenation.—The treatment of cardiac standstill is primarily that of giving oxygen and the production of systoles by rhythmical compressions of the heart. The importance of oxygenation to the lungs cannot be overstressed, and this is best accomplished by intermittently fully distending the lungs and then deflating at the rate of 20 to 30 per minute, preferably with an intratracheal catheter. Respirators such as the E and J, the Mautz, or similar types are suited for this purpose. Anesthetists today are quite adept at performing mechanical respiration by rhythmic compressions of the rebreathing bag. Caution must be exercised not to use excessive pressure, preferably not over 16 mm. of mercury, in order to avoid damage to the lungs. Where other means are not available, mechanical compressions of the chest with traction on the tongue, or even direct insufflation with the mouth over cupped hand should be used. The patient should also be placed in slight Trendelenburg position to facilitate circulation.

Restoration of Cardiac Action.—The first attempt at resuscitation after the head has been lowered and artificial respiration started may consist in the breaking of an amyl nitrite pearl under the patient's nostril. An intracardiac injection of 1 c.c. epinephrine in cases of cardiac standstill (but not where ventricular fibrillation is suspected) is given in the left fourth interspace near the sternum. While this is being done, if the abdomen is not already open, the chest and abdomen should be hastily painted with skin solution. The upper abdomen should be quickly opened and the right hand passed up under the diaphragm below the heart while the left hand is put on the chest wall over the cardiac area. The right hand under the diaphragm compresses the heart against the chest wall in a squeezing motion between it and the hand on the chest wall. Forty to 60 compressions per minute should be used, and if by the end of one minute of this procedure no response is obtained, the diaphragm should be opened beneath and to the left of the ensiform cartilage and the hand introduced into the chest cavity where the heart can be grasped with the hand and contractions continued. Elevation of the feet will furnish additional blood. If the anesthetist is ventilating the lungs, oxygenated blood will then be forced to the brain even though the heart itself does not contract automatically. If after the

elapse of another minute the heart has not resumed contractions or if the heart can be felt to be fibrillating, the costal cartilages are cut so the heart can be visualized. Massage should not be discontinued until automatic heart action is restored as the patient can be kept alive by manually forcing the heart to beat. When the heart action is restored, the opening in the chest and abdomen is closed and the patient is carefully watched until heart action and blood pressure are stabilized.

In ventricular fibrillation resuscitation becomes more difficult as the hyperirritable heart usually will not respond favorably to massage alone. First the cardiac musculature must be made less irritable by the use of 2 per cent procaine intravenously, or an injection of 4 to 10 c.c. into the right auricle. Topical application of procaine to the heart is also advisable. If this fails there is an alternative procedure of defibrillating the heart with an electric current as advocated by Beck. The 1½ amp. 110 volt current which is applied to the heart through 2 large metal electrodes for 0.1 to 0.5 second shocks the heart to produce a state of contraction after which it should relax and not show any movement. Massage is then started. Where response to massage is slow, Beck has advised the use of 1 c.c. epinephrine and 5 c.c. of 1 per cent calcium chloride into the right ventricle.

CASE 1.—M. J. was a 59-year-old Mexican woman with extensive invasion of epidermoid carcinoma of the left eyelid, invading the orbit. Preoperative medication consisted of morphine, gr. ¼, scopolamine, gr. 1/200, one-half hour prior to surgery. The anesthetic was Pentothal Sodium, and a total of about .4 Gm. was given. A thorough preoperative preparation of the eye was performed while the anesthetist shielded the normal eye. This took an estimated 6 minutes. Upon completion of the preparation, it was noted that the patient's color was very pale and respiration had ceased. Artificial respiration was immediately instituted by compressing the rebreathing bag of the anesthetic machine, using pure oxygen. After a minute or so her color did not improve nor was breathing restored. Auscultation of the heart revealed the absence of heart action. The abdomen and chest were quickly painted, and an upper abdominal incision just to the left of the midline was made. With the right hand under the diaphragm and the left hand over the chest wall, the heart, which was relaxed and not beating, was massaged and compressed against the anterior chest wall. After one-half to one minute, faint contractions were felt and massage was continued, and within 2 minutes more full automatic heart action was restored. After closure of the abdomen, the patient was returned to the ward. She had a perfectly normal convalescence. One week later the operation for removal of the malignancy was performed, and her recovery was uneventful.

CASE 2.—J. M., a 45-year-old Mexican man, was a patient upon whom a partial gastrectomy was being done for obstruction as a result of a peptic ulcer. Spinal anesthesia had been used, supplemented by pentothal. When the duodenal stump was closed and about three-fourths of the stomach had been mobilized, the anesthetist suddenly noted that the patient was not breathing. No pulsation of the abdominal aorta could be felt. Forced ventilation of the lungs was performed by compressing the rebreathing bag. An immediate atempt was made to massage the heart through the diaphragm, but no response was obtained. The chest was then opened and the diaphragm was severed from the anterior chest wall sufficiently to get a hand into the chest, without opening the pericardium. Massage of the heart was started, and after 1½ minutes of massage, we were able to obtain a few feeble heartbeats. About this time the oxygen gave out. Artificial respiration with airway in the mouth was given, and the massage continued until full heart action was restored. More oxygen was soon obtained and the patient's blood pressure returned

to normal. The gastrectomy was completed and the patient returned to his room in good condition. The postoperative convalescence was uneventful, and the patient is now living and well. Recovery of heart action in this case was obtained by massage and artificial respiration only, as no drugs were administered.

CASE 3.—G. F., a 66-year-old white woman developed cardiac arrest immediately following introduction of the endotracheal tube under cyclopropane anesthesia preparatory for a laparotomy for gallstone ileus. An upper midline incision was made immediately, and a subdiaphragmatic massage was started. Since there was inappreciable response, the incision was extended upward along the costal cartilages and the pericardium opened. Fine fibrillary twitchings of the ventricle could be seen. Twenty-four minutes after initiation of massage, following continuous massage and use of Adrenalin, Novocain, and atropine, radial pulse could be felt faintly. Repeated use of these drugs in addition to Cedilanid and Coramine together with repeated massage improved the cardiac status so that after 53 minutes radial pulsations became constant and autonomous. This condition was maintained for approximately 54 minutes and an attempt was made to close the chest and abdomen, when ventricular fibrillation recurred. Despite further efforts at resuscitation it was no longer possible to bring the heart back to autonomous action. Autopsy examination revealed old healed infarcts in the apex of the heart as well as multiple new hemorrhagic areas in the myocardium.

CASE 4.—A. C., a 27-year-old woman, had cephalopelvic disproportion. Because of this a low cervical cesarean section was performed by one of us (H. G. B.) under pontocaine spinal anesthetic a few days before term. Ephedrine, ¾ gr., was given subcutaneously just before the anesthetic. No other sedation was used. Brief but brisk bleeding not exceeding 400 to 500 c.c. resulted from a low-lying anterior placenta. (The baby reacted promptly and was held up for the mother's inspection. She commented briefly on the experience.) Ten units of Pituitrin were then injected into the uterus, and $\frac{1}{320}$ gr. of Ergotrate was given intravenously, and closure of the uterine incision commenced. The patient complained of faintness and was apprehensive. This was 30 minutes after administration of the spinal anesthesia. Oxygen inhalation was commenced, but the patient ceased to breathe and cardiac action ceased. Artificial respiration was started by rhythmical compression of the rebreathing bag. Ephedrine, ¾ gr., was given intramuscularly. After several minutes without response (no time record was kept) the heart was palpated through the diaphragm and found to be motionless. Rhythmical compression of the heart was immediately commenced through the diaphragm. The patient's color promptly improved, and after about 20 minutes, single contractions began, infrequently at first, but gradually increasing until regular rhythm was established. Jerky, irregular respiration commenced 15 to 20 minutes after restoration of heart rhythm. This finally became regular, the blood pressure reached 100 mm. systolic, and the patient's color was good. When moved from the operating room there was generalized mild spasticity with occasional fibrillary spasms involving at first the facial muscles and finally resulting in convulsions. Twenty-seven hours after surgery the blood pressure was 130/80 and the pulse strong and regular. Thirty-two hours after surgery the patient died with pulmonary edema and circulatory failure, having never regained consciousness.

Autopsy diagnosis was: (1) acute myocardial infarction, cause unknown; (2) patchy pneumonia; (3) bilateral atalectasis; and (4) hypostatic congestion.

In this case the sudden onset of cardiac arrest occurring shortly after the administration of Pituitrin into the uterus seems to point to Pituitrin as the probable cause of cardiac arrest. In spite of the rarity of serious or fatal Pituitrin shock, its possibility should be kept in mind; when Pituitrin is used, it is best not to administer it intravenously, or into the gravid uterus at the time of surgery.

SUMMARY AND CONCLUSIONS

Management of cardiac arrest can be summarized as follows:

1. In cardiac standstill the management should include (a) oxygen; and (b) massage of the heart.

2. In ventricular fibrillation the management should include (a) oxygen; (b) defibrillation with the use of procaine or electric shock; and (c) massage.

The use of epinephrine has been controversial. We feel, however, that it may be used in conjunction with massage as long as fibrillation is not present.

In our experience, the 2 successful cases of cardiac massage were performed without the aid of any medication. On the other hand, in the 2 unsuccessful cases, we encountered failure despite all medications and effort. A common cause of failure is delay in instituting active treatment.

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FAILURE OF A DOUBLE JEJUNAL LUMEN GASTROJEJUNAL ANASTOMOSIS TO PROTECT AGAINST THE HISTAMINE-PROVOKED ULCER

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ONE of the most troubling complaints after gastric resection is the occurrence of the so-called dumping syndrome. A common explanation for it is that it is partly due to the rapid distention of the gastric pouch and intestinal loop after eating. In an attempt to prevent that complication, Steinberg[6] proposed the use of a variation of the normal gastrojejunal anastomosis, whereby a latero-lateral jejunojejunostomy, made at the outlet of the stomach, would provide an additional pouch, increasing the reservoir capacity of that organ. Steinberg also thought that this particular type of anastomosis would prevent the regurgitation of bile and pancreatic juices in the stomach. It has been shown by Wangensteen and his collaborators,[4, 7, 9] McCann,[5] and Kesavalu and Mann[3] that the complete regurgitation of those alkaline juices in the stomach—by a Schmilinsky-type of procedure—does not produce a complete neutralization of the gastric content. Instead, the gastric acidity remains high, and jejunal ulcers occur quite frequently. In the course of his study, Steinberg conducted some experiments with injections of histamine-in-beeswax on 3 dogs, subjected to a gastrojejunostomy with a double jejunal type of anastomosis. He observed ulceration in 1 dog only, and concluded that this type of anastomosis prevents the appearance of jejunal ulcers.

The present report concerns observations regarding the possibility of ulcer prevention by this double-lumen type of anastomosis.

METHODS

The experiments were carried out on 6 dogs in 2 series. In series I, a gastrojejunostomy with double jejunal lumen anastomosis was performed on 3 dogs. In series II, a 50 per cent gastric resection was performed, and the gastrointestinal continuity re-established by a gastrojejunostomy with double jejunal lumen anastomosis. After an interval of 4 weeks, the histamine-in-beeswax mixture, prepared after the method of Code and Varco,[1] was administered. A dose of 30 mg. of histamine-base was injected intramuscularly each evening, about 5 P.M. Following the injection, the feed pans were removed, and no food was allowed until the next morning. The dogs were given histamine-in-beeswax for a period of 45 days, unless they died in the interval.

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*Graduate Fellow of the Belgium American Educational Foundation.

OPERATIVE PROCEDURES

All operations were done under intravenous Nembutal anesthesia and aseptic conditions. During the first 3 postoperative days no food was given, and the dogs were supported by daily infusions of Ringer's and glucose solutions. Penicillin, 50,000 units, was injected intramuscularly twice daily during the same period.

Gastrojejunostomy.—On the first 2 dogs of this series (Table I) an open anastomosis was done, following the technique described by Steinberg. After division of the ligament of Treitz, the afferent and efferent branches of the first jejunal loop were joined together and an open laterolateral jejunojejunostomy was done on the distal half, using 2 rows of sutures: continuous 000 catgut for the inner one and interrupted 0000 silk for the outer one. Using the same type of open anastomosis, the proximal half of the created jejunal pouch was then anastomosed to the greater curvature of the stomach. For the third dog of this series (Dog 3, Table I) an aseptic anastomosis was done, following Wangen-

Fig. 1 (Dog 2).—Stoma ulcer after 50 per cent resection following double jejunal lumen anastomosis (see Table II).

steen's technique.[8] A laterolateral jejunojejunostomy was done on the distal half of the afferent and efferent branches of the first jejunal loop, and the proximal part of the pouch was anastomosed to the greater curvature of the stomach. In all 3 cases, the distal point of the jejunal pouch was always at the level of the divided ligament of Treitz; the length of the jejunal pouch was 5 cm; the gastrojejunostomy opening was 3 cm. in diameter in 1 case, and 4 cm. in 2. It was placed on the greater curvature between 4 and 6 cm. from the pylorus.

Fifty Per Cent Gastric Resections.—In all 3 cases of this series, an aseptic anastomosis was done, with one row of 0000 silk throughout. The distal half of the stomach was resected, the duodenal stump closed, and the jejunal pouch anastomosed to the stomach following the Polya modification of the Billroth II pattern. In all 3 dogs, the distal point of the jejunal pouch was at the level of the divided ligament of Treitz; the length of the pouch was 6 cm., and the diameter of the gastrojejunostomy was 4 cm. in 2 cases and 5 cm. in 1.

RESULTS

The incidence of histamine-in-beeswax-provoked jejunal ulcers and erosions following gastrojejunostomy or 50 per cent gastric resection with a double jejunal lumen anastomosis is shown in Tables I and II. Out of 3 dogs with a gastrojejunostomy, 2 had ulcers, of which 1 perforated on the eighteenth day. The 3 dogs with 50 per cent gastric resection all had ulcers. Two perforated (on the fourth and fifth days respectively), and a massive hemorrhage occurred in 1 (on the ninth day).

TABLE I. INCIDENCE OF JEJUNAL ULCERS IN DOGS FOLLOWING GASTROENTEROSTOMY WITH A DOUBLE JEJUNAL LUMEN ANASTOMOSIS

DOG NUMBER	WEIGHT (POUNDS)	NUMBER OF INJECTIONS	RESULTS	REMARKS
1	16	45	No ulcer	Sacrified on 46th day
2	24	18	3 ulcers in intestinal pouch, 1 perforated; 2 erosions in afferent loop	Died, peritonitis
3	29	30	2 ulcers, 1 in jejunal pouch, 1 in efferent loop; numerous erosions in efferent loop.	Died, bilateral bronchopneumonia

TABLE II. INCIDENCE OF JEJUNAL ULCERS IN DOGS FOLLOWING 50 PER CENT GASTRIC RESECTION WITH A DOUBLE JEJUNAL LUMEN ANASTOMOSIS

DOG NUMBER	WEIGHT POUNDS	NUMBER OF INJECTIONS	RESULTS	REMARKS
1	35	4	4 ulcers in jejunal pouch, 1 perforated; numerous erosions in efferent loop	Died, peritonitis
2	28	9	1 erosion and 2 ulcers in pouch, with an eroded artery in one of them (Fig. 1)	Died, massive hemorrhage; jejunum and ileum filled with fresh blood
3	25	5	1 ulcer in jejunal pouch, perforated	Died, peritonitis

DISCUSSION

Lannin, in 1945,[4] performed simple gastrojejunostomies and 50 per cent gastric resections in dogs. Of 4 dogs with gastrojejunostomies, all had jejunal ulcers. Two died of perforation and generalized peritonitis on the third and thirteenth days, and 2 were sacrificed after 40 injections of histamine-in-beeswax. Of 4 dogs with 50 per cent gastric resection, only 1 had a stomal ulcer with perforation. One had jejunal erosions, and 2 had a normal stomach and jejunum after 40 injections of histamine.

By comparing Lannin's series and the present experiments, it becomes apparent that the addition of a double jejunal lumen to a gastrojejunostomy or a 50 per cent gastric resection does not increase the protection against the histamine-provoked ulcer. On the contrary, it seems that the double jejunal lumen facilitates ulcer production. In our series, ulcers were found more frequently, appeared sooner, and were more severe than in Lannin's series, where a simple lumen anastomosis was done.

These results agree with our present knowledge about stomal ulcer formation and prevention. The development of a jejunal ulcer is the result of the

attack by the acid-peptic juice on the highly sensitive jejunal mucosa. After gastric resection, the constant flow of bile and pancreatic juices on the jejunal mucosa undoubtedly affords protection against the digestive action of the gastric juice. Any type of surgical procedure that diverts those alkaline juices from the anastomosis will decrease the resistance of the jejunal mucosa and facilitate ulcer formation. In 1911, Exalto[2] showed that a gastrojejunostomy of the Roux-Y type leads to the development of stomal ulcers in a high percentage of cases (6 out of 7 dogs). In his experiments, also, the addition of a jejuno-jejunostomy between the afferent and efferent loops increased the frequency of jejunal ulceration. It is our opinion that the double jejunal type of anastomosis, if made long enough to form a reservoir at the outlet of the stomach, acts then as a laterolateral jejunojejunostomy, side-tracks the alkaline duodenal content from the anastomotic line, and in consequence, decreases the resistance of the jejunal mucosa.

CONCLUSION

The addition of a double-lumen jejunal pouch to a gastrojejunostomy or a 50 per cent gastric resection fails to protect against the histamine-provoked ulcer in the dog.

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AN ORIGINAL DRAINAGE APPARATUS FOR ILEOSTOMIES AND FISTULAS

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A NEW type of ileostomy apparatus has been devised which has many advantages over previously constructed appliances. It has been employed for several months by four patients with ileostomies, one with cutaneous ureterostomies, and by another with a colostomy into which both ureters had been implanted.

DESCRIPTION OF THE APPARATUS†

The apparatus (Fig. 1) consists of the following items:

1. There is a 5 inch rubber disc with a centrally placed mouth. The mouth, which is 13 mm. deep, flares away from the fistula. The center of the disc may be easily cut to conform to the size and shape of any enterostomy. The outward flare militates against stagnation of waste products between the ileostomy and the inner aspect of the mouth and allows complete emptying. The outer contour of the mouth assures a snug fit of the rubber band around the neck of the polyethylene bag. Since a minimum area of rubber is exposed to fecal drainage, odor and deterioration of the rubber are markedly reduced.

2. Adhesive Pro-cap‡ discs are doubly backed with polyethylene and have a long-lasting adhesive property. Pro-cap adhesive has been shown to cause less irritation because of the addition of zinc salts of proprionic and caprylic acids.[1]

3. A nonbreakable, pure rubber band fastens the bag securely to the neck of the rubber disc. No leakage has occurred in any of the six patients upon whom this apparatus has been tried.

4. The disposable, inexpensive polyethylene bags§ can be flushed down the toilet.

5. A belt made of waterproof webbing attached to a plastic ring holds the rubber disc securely against the body.

COMMENT

The apparatus has been applied as early as the fifth postoperative day at the time of withdrawal of the catheter from the ileostomy (Figs. 2 and 3). Unlike one-piece rubber ileostomy bags, this unit enables the physician to observe

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†The entire apparatus can be procured from Thomas Fazio, 1878 Commonwealth Ave., Auburndale 66, Mass.

‡Manufactured by the Seamless Rubber Company, New Haven 3, Conn.

§The bags consist of Visqueen film made by Visking Corporation, New York.

the appearance of the exteriorized bowel and the contents of the bag without disconnecting the apparatus.

The rubber disc has adhered to the skin of the patients with ileostomies and to the skin of the patient with cutaneous ureterostomies for as long as eight

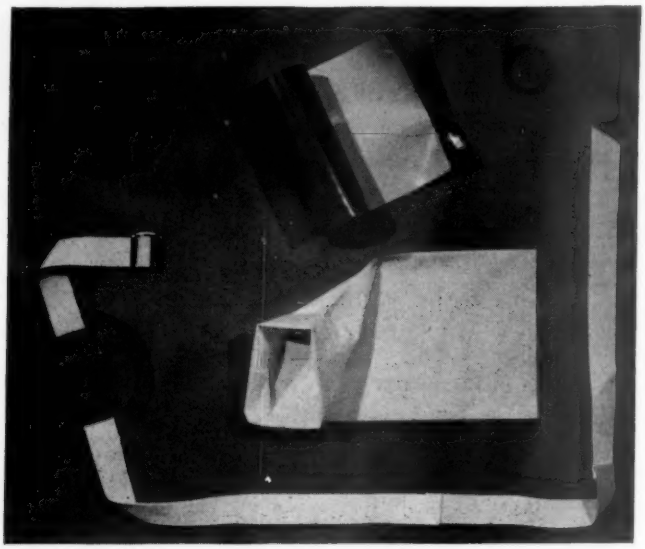

Fig. 1.—Beginning in the upper left-hand corner and proceeding clockwise the following are seen: (1) the rubber disc; (2) the adhesive tape backed with polyethylene; (3) the rubber band; (4) the disposable polyethelene bag; and (5) the belt.

Fig. 2.—Apparatus without the belt in place on the seventh day after construction of an ileostomy. The string under the rubber band facilitates removal of the latter. The distal ileum can be seen in the left paramedian incision.

days. Heretofore, the patient with a colostomy into which both ureters have been implanted has presented a formidable problem to the surgeon because of his inability to control leakage and excoriation of the skin. In a recently treated

patient with a "wet colostomy" the rubber disc has adhered to the skin for thirty-six to sixty hours at a time. After the first application, a complete subsidence of irritation of the skin was noted. In none of the patients treated has there been any evidence of skin irritation. This was true even in a patient with an ileostomy whose skin was sensitive to all other types of adhesive.

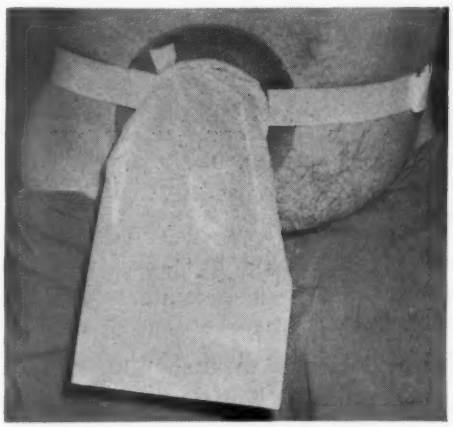

Fig. 3.—The complete apparatus can be seen in place.

SUMMARY

A new apparatus which can be applied to any type of fistula has been described. Its main advantages can be attributed to a tenaciously adherent, nonirritating, double-backed adhesive and to easily disposable, nonodorous, inexpensive polyethylene bags.

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THEORETICAL HAZARDS IN THE TREATMENT OF PATHOLOGIC FRACTURES BY THE KUNTSCHER INTRAMEDULLARY NAIL

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INTRODUCTION

THE place of intramedullary nailing in the treatment of pathologic fractures of the long bones, especially the femur, has been well illustrated in this country by the work of Ehrenhaft and Tidrick.[6] Fractures associated with a variety of secondary bone tumors have been treated by this method (Table I), and intramedullary nailing has been recommended for use in this group of fractures by Cave.[4]

To fix a pathologic fracture by means of an intramedullary nail involves a disruption of the entire marrow cavity and the transfixion, by the nail, of an area containing tumor cells. Important corollaries of this procedure are: (1) the problem of seeding the local area with tumor cells, and (2) the possibility of widespread dissemination of tumor cells by embolization. It is the purpose of this paper to discuss these basic hazards inherent in the operative procedure.

EXPERIMENT I*

This experiment was designed to demonstrate whether or not cells, in this case bacteria, could be spread within the marrow cavity by the passage of an intramedullary nail.

A series of glass tubes (2 by 50 cm.) was prepared under sterile conditions, each tube containing a 35 cm. high column of tryptase-peptonized milk, a semi-solid medium. At the mid-point of this sterile column was interposed an area of medium 2 cm. long containing a heavy suspension of *Bacteroides tumidus* (American Type Culture Collection 8496), gram-negative rods, obligate anaerobes, ideally suited for growth in deep cultures.[2] Sterile intramedullary nails, 1 by 40 cm., of hollow clover-leaf design† were then inserted into the tubes and passed through the agar column, transfixing the inoculum. The tubes were then incubated at 37° C. and examined at 24 and 48 hours.

At the end of 24 hours, the area of the inoculum remained well delimited and bacterial growth could be detected in small amounts for not more than 3 cm. below this point. At the end of 48 hours, bacterial growth had become evident in all the tubes throughout the entire column of agar below the area of the inoculum (Fig. 1).

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†Supplied by the Zimmer Manufacturing Company, Warsaw, Indiana.

TABLE I. SECONDARY BONE TUMORS CAUSING FRACTURES TREATED BY INTRAMEDULLARY NAILING

Epithelioma[20]
Carcinoma of the alveolar ridge[6]
Carcinoma of the breast[6, 7, 15]
Carcinoma of the thyroid[5]
Carcinoma of the renal cortex[6, 9]
Multiple myeloma[6, 20]
Carcinoma of the lung[7]

The nail in passing through the area of inoculum picked up sufficient bacterial cells to inoculate the entire distal column of agar. An entirely similar method of inoculation is used in making routine cultures of anaerobic organisms by stabbing the inoculum into deep agar tubes with a straight inoculating needle.

EXPERIMENT II*

This experiment was designed to demonstrate the movement of cellular emboli within the marrow cavity of a long bone after the insertion of an intramedullary nail.

Human red blood cells were tagged with radioactive phosphorus in the following manner. Fresh blood, 20 c.c., was placed in an oxalated tube, and c. 50 microcuries of P^{32} were added. The tube was incubated in a constant temperature bath at 37° C. for 2 hours. Following this the blood was centrifuged for 30 minutes at 3,000 r.p.m. and the supernatant plasma removed. The cells were resuspended in normal salt solution and centrifuged again. This washing process was repeated several times and the decanted supernatant fluid was monitored with a Geiger counter until no appreciable radioactivity remained in the washings. The cells were then used immediately for the experiment.

Fresh human tibias, obtained from patients undergoing amputations for peripheral gangrene, were removed with careful preservation of the periosteum. At the mid-point of the shaft, a hole was made through the cortex and threaded to receive a one-half inch pipe plug, to act as a water-tight, pressure-resistant seal. Smaller holes were then made in the cortex at 5 cm. intervals, proximally and distally from the plug. These holes snugly received needles (No. 15) 3 cm. long. The tibial plate was pierced with a drill in the region of the tibial spines to facilitate the insertion of an intramedullary nail.

A small sample of the prepared blood cells was taken as a control. The contents of the marrow cavity of the tibia immediately beneath the plug were removed and the space filled with 2 or 3 c.c. of the red blood cells. The plug was then screwed firmly in place. A hollow clover-leaf nail (1 by 40 cm.) was then driven into the upper end of the tibia, passing through the entire length of the marrow cavity. During the nailing, the bone marrow flowed from the needles in the cortex and was collected in small aluminum planchets. Marrow draining from the point of entrance of the nail was also collected.

*The P^{32} used in this experiment was obtained from Oak Ridge, Tenn., and was made available to the author by Dr. Jun-Chuan Wang, Department of Radiology, University of Minnesota Medical School. His help and cooperation in this experiment was greatly appreciated.

The radioactivity of the collected material was determined using a mica window Geiger counter with a planchet-window distance of less than 1 cm. At least 1000 counts were recorded for each sample. Background counts were taken and used to correct final data. No corrections were made for decay or self-absorption.

When red blood cells are tagged in this manner and used immediately, almost all of the P^{32} is contained within the cell or adsorbed upon its surface.[12] For this reason, the presence of radioactive material in the samples collected from the marrow is considered to demonstrate the presence of the tagged cells in the sample. Using control samples, it is possible to roughly estimate the number of cells present in relation to the amount of radioactivity. As can be seen from Fig. 2, considerable amounts of radioactive material were widely distributed both proximally and distally in the marrow cavity. The distribution in the marrow cavity was irregular. The highest count was obtained from material exuded from the nutrient artery of the tibia in one case.

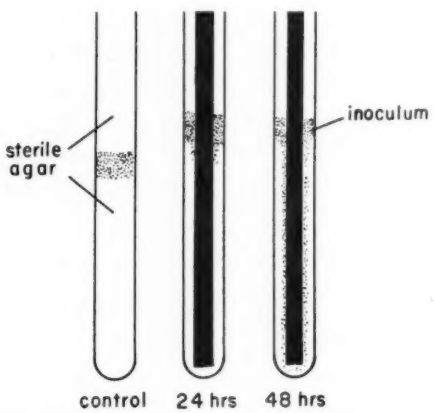

Fig. 1.—This drawing summarizes the results of the bacterial cultures in Experiment I. At the end of 48 hours, growth was evident in all tubes to the end of the nail.

DISCUSSION

The first pathologic fracture treated by intramedullary nailing was caused by a metastatic carcinoma of the renal cortex. Seven months after the operation, roentgenograms showed an extension of the osteoclastic process in both directions, but especially distally, from the site of fracture. Haase[9] concluded from this that the passage of the nail had distributed tumor cells up and down through the marrow cavity. Moeys[15] reviewed 5 cases of pathologic fracture resulting from metastatic carcinoma of the breast in which nailing had been performed. In each case the entire bone was examined carefully at necropsy. In one patient, tumor cells were found to have spread to the distal end of the nail. He concluded that tumor cells could be spread by the insertion of the nail, the direction depending upon the technique of insertion. An analogy can easily be drawn between the marrow cavity of a long bone containing a focus of metastatic tumor and a tube of agar containing a focus of bacterial cells. Are the tumor cells carried into the distal fragment of the bone by the passage of the nail? I think so.

Following intramedullary fixation of fractures of the femur, a small calcified cap or kallushütchen sometimes appears over the proximal end of the nail in the trochanteric fossa (Fig. 3). It is composed of fibrous tissue, bone and cartilage, and bone marrow elements.[1] This cap represents the growth of cellular material displaced from the marrow cavity by the nail, and flowing

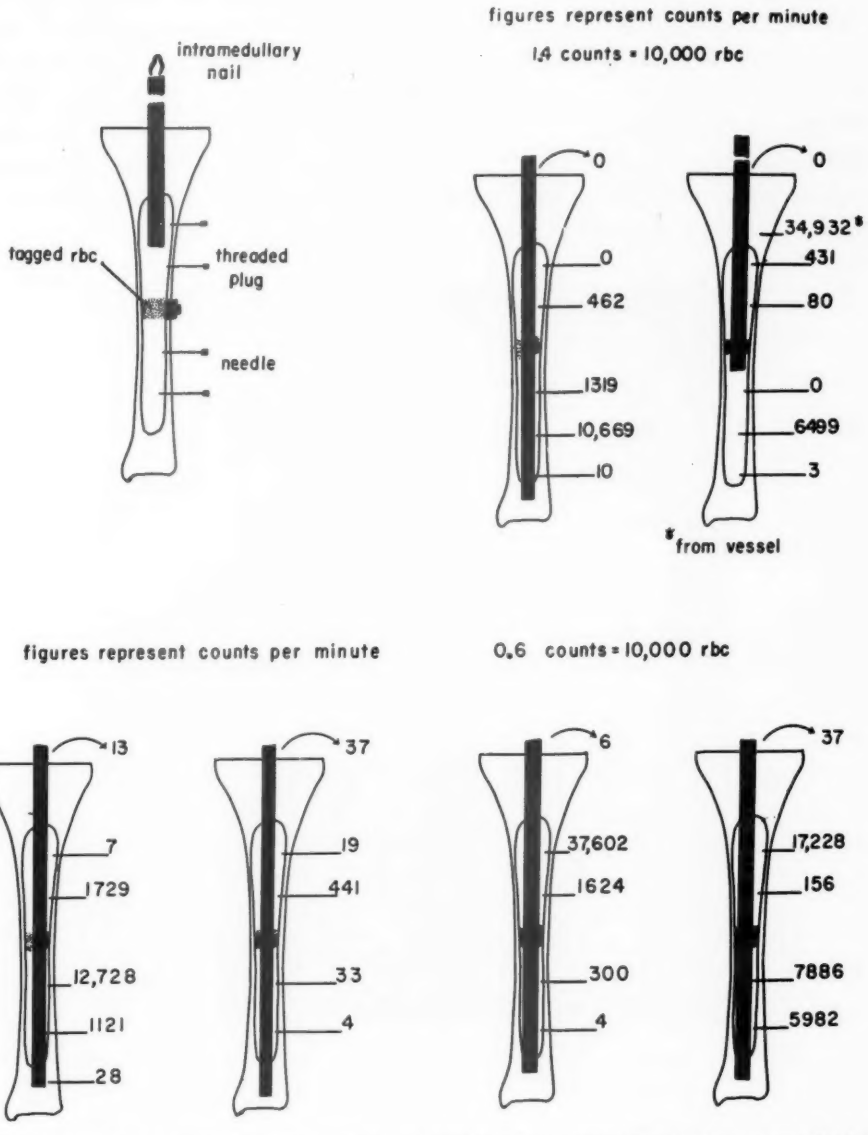

Fig. 2.—This drawing illustrates the method of performing Experiment II as described in the text, and summarizes the data obtained.

through the cortex along the gutter of the nail. Such a flow of marrow is commonly observed at operation. Although no clinical reports of tumor masses occurring in the trochanteric fossa have appeared, in examining a patient for evidence of spread or recurrence of the tumor after nailing the trochanteric fossa and its contents about the proximal end of the nail should be carefully scrutinized.

Three conditions essential for the production of cellular emboli by trauma are: (1) rupture of the tissue stroma, (2) the presence of open venous channels communicating with the general circulation, and (3) an increase in the local tissue pressure which acts to move the emboli into the venous channels. These conditions form the common denominator in the reported cases of: (1) liver emboli, found in the lungs following crushing injuries of the liver,[11] (2) emboli of brain tissue found in the lungs following severe head injuries,[11] and (3) emboli of placental cells, amniotic fluid, and meconium particles following difficult deliveries.[8, 11, 19, 22] Fat embolism regularly occurs under similar circumstances following bony injuries. Bone marrow emboli appear in the lungs in association with fat emboli.[11, 13, 18, 21] Fat cells, megakaryocytes, myelocytes, erythroblasts, and pigment cells have all been described as appearing in the pulmonary vessels following trauma to the bone.[11]

Fig. 3.—This roentgenogram of the hip of a patient was made 2 months after internal fixation with an intramedullary nail for fracture of the shaft. A well-formed and calcified cap (the so-called kallushütchen) can be seen over the end of the nail.

The insertion of an intramedullary nail into the marrow cavity of a long bone produces extensive disruption of the tissue. Vascular spaces and venous channels are opened and numerous avenues into the general circulation become available. A sudden large increase in the local tissue pressure occurs, furnishing the *vis a tergo*. This pressure varies somewhat with the design of the nail employed.[16] It is not surprising, therefore, that a slight degree of fat embolism occurs regularly following intramedullary nailing.[7, 14] A few deaths attributed

to fat embolism have occurred after intramedullary fixation.[1, 3, 10] Under conditions such as these, the coincident appearance of cellular emboli from the marrow cavity following nailing becomes a real possibility.

It would appear from a careful examination of the data from Experiment II (Fig. 2) that the movement of such large numbers of cells and their irregular distribution can best be explained on the basis of embolization. This mechanism is probably of major importance in spreading tumor cells in the bone, although direct movement with the nail, as illustrated in Experiment I, does undoubtedly occur. All of the cellular emboli produced are not confined to the local area. A portion must enter the general circulation and reach the lungs. The fate of such emboli has recently been noted by Saphir.[17] It has been known for many years that tumor emboli do not always produce metastases.[11] However, traces of their sojourn in the lungs can be found on careful microscopic examination. It only remains to say that diffuse metastases in the lung and elsewhere are most commonly due to tumor cell emboli.[23] Certainly the production of tumor cell emboli during an operative procedure may place the patient in considerable jeopardy.

CONCLUSIONS

Bacterial cells can be spread by the passage of an intramedullary nail through a culture medium in the same manner as with an inoculating needle.

Red blood cells tagged with P^{32} can be widely spread both distally and proximally in the marrow cavity of the tibia by the insertion of an intramedullary nail.

Clinical evidence of such spread of tumor cells has been cited.

Although cells can be moved by adsorption to the passing nail, the production of emboli is of the most importance in the movement of cells.

The local spread of tumor cells in the bone and the possibility of widely disseminated tumor emboli following intramedullary fixation of pathologic fractures of the long bones are of real importance in planning the proper care of the patient.

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Case Reports

SKIN GRAFT FOR PROLAPSE OF ILEOSTOMY

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PROLAPSE is one of the most troublesome complications of ileostomy. It may involve only the mucosa of the ileum or it may involve all layers of the wall, forming an intussusception. The first variety rarely causes serious difficulty, but may progress to the second type. In the second type there is an extrusion of varying lengths of ileum which may result in partial obstruction and may terrify the patient. As a rule the prolapse will reduce itself when the patient lies down, only to recur when the patient stands.

In a preliminary report in 1941, Dragstedt[1] described a method of applying a split-thickness skin graft to an end ileostomy. In more recent discussions Black and Thomas[2] described 4 cases, Sanders[3] reported 5 cases, and Bartlett and Peck[4] described 2 in which grafts were applied. The main objective of this procedure is to carry the ileal contents away from the abdominal wall, and to prevent excoriation of the skin.

The following is the report of a case in which a skin graft was applied to prevent recurrent prolapse of an ileostomy.

REPORT OF CASE

On Dec. 2, 1948, a 29-year-old woman with ulcerative colitis of 8 years' duration was admitted with an exacerbation of the disease. She was acutely ill and did not respond well to medical treatment.

A loop ileostomy was done on December 16, and following this her condition improved.

Approximately 3 months later she was again admitted to the hospital complaining of prolapse of her ileostomy. She said the prolapse had occurred for the first time as she was lifting something at home. It was becoming progressively larger and more difficult to reduce. When the prolapse occurred again 18 inches of prolapsed ileum were amputated, and an end ileostomy was created.

She wore a Rutzen bag and did well until about 7 months later, when she returned complaining of recurrence of the prolapse, which had started soon after the last operation and which gradually enlarged until it protruded over 8 inches.

On Nov. 4, 1949, the ileostomy was freed from its attachments to the abdominal wall and pulled up so that about 2 inches protruded through the abdominal incision. A split-thickness skin graft was taken from the right thigh and trimmed to fit around the ileum. The graft was joined to itself with 000 plain catgut, and was anchored lightly to the skin of the abdomen with 5 fine silk sutures. A catheter was placed in the ileum to carry away the intestinal contents, and was removed on the fourth postoperative day. The graft showed an almost 100 per cent take, and was protected from then on with aluminum paste. She was discharged on the eighth postoperative day wearing the Rutzen bag.

Following discharge she had no recurrence of the prolapse, but was troubled with partial obstruction of the ileostomy, which necessitated catheterization in order to allow the contents to escape freely. On examination it was felt that the abdominal incision

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was closed too tightly. On Dec. 28, 1949, the abdominal opening was enlarged slightly. Following this procedure the ileostomy has functioned well, and the prolapse has not recurred. It is now 6 months since operation.

SUMMARY

A case is reported in which prolapse of an end ileostomy was successfully treated by application of a Dragstedt type of skin graft.

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TRAUMATIC PERFORATION OF THE RECTOSIGMOID COLON

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PERFORATION of the rectum or rectosigmoid is relatively uncommon. This is usually done with a sigmoidoscope, an enema tip, or a thermometer. Occasionally self-introduced objects will cause perforation. However, perforation and entrance of the foreign body into the general peritoneal cavity with transabdominal removal is a much rarer occurrence. Only three reported cases were found in the literature.

The case presented below is one of perforation through the rectosigmoid by a self-introduced foreign body.

CASE REPORT

F. A. (Lincoln Hospital No. 2778-50), a 68-year-old man, walked into the emergency room at 11:30 A.M., Mar. 13, 1950, complaining of severe abdominal pain. The patient stated that at 9:30 A.M. the morning of admission he inserted a well-lubricated bottle, large end first, into the rectum. The patient stated that he did this to relieve constipation and was in the habit of doing this about once a month. A string attached to end of bottle broke and the bottle slipped out of reach. The patient had severe abdominal pain at this time. In order to try to retrieve the bottle he took an enema by attaching a piece of hose directly to a water faucet. But the water did not wash the bottle out. He then noticed moderate bleeding from the rectum and increased pain. He then dressed and walked ten blocks to the hospital.

His past history was noncontributory. An appendectomy had been done thirty-five years previously, and a hemorrhoidectomy eighteen years previously. The patient was unmarried and lived alone.

Physical Examination.—The patient, an elderly white man, pale and cool, complained of abdominal pain. Blood pressure was 120/90, pulse 110. Physical examination was normal except for abdominal examination. The abdomen was moderately distended, rigid over all quadrants, and extremely tender. Deep palpation was prevented by boardlike rigidity. Rectal examination revealed red blood on the examining finger. The foreign body was not palpable.

Urine examination was negative. A flat film of the abdomen showed a large glass bottle in the left side of the abdomen (Fig. 1).

Course.—Because of the physical findings of peritonitis it was assumed that the bottle had perforated the rectosigmoid. The patient was prepared for laparotomy and a blood transfusion was started. Under spinal anesthesia (Pontocaine and glucose) the abdomen was opened through a lower left rectus muscle-splitting incision. The peritoneal cavity contained about 800 c.c. of serosanguineous fluid mixed with blood clots and occasional pieces of feces. This was removed and the tear in the rectosigmoid visualized. A three-inch longitudinal laceration was seen at the distal end of the sigmoid. The sigmoid could not be completely mobilized. The tear was repaired by two layers of fine chromic sutures. The wound was closed in layers, and reinforced with four tension sutures of heavy silk. Because of the contamination of the peritoneum and to protect the colon suture line, a gas vent was provided by a tube cecostomy through a right McBurney muscle-splitting incision.

Postoperatively the patient received penicillin and streptomycin. He did well, the bowels moving on the fifth postoperative day. On the eighth postoperative day the cecostomy tube was removed. On the tenth postoperative day his temperature rose to 102° F. and a pelvic cellulitis was felt by rectum. The patient was placed on aureomycin and the cellulitis subsided in four days. The cecostomy wound healed rapidly and the patient was discharged on the nineteenth postoperative day.

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Comment.—Because of the clean laceration of the colon, primary suture was done. The need for cecostomy was debatable, but because of the established peritonitis and the danger of an ileus which might jeopardize the suture line, a tube cecostomy was done. It was felt that the antibiotics, especially aureomycin, aided in the prevention of a pelvic abscess or a more severe peritonitis.

Fig. 1.—Flat film of the abdomen, showing the bottle in the left side of the abdomen.

SUMMARY

A case is reported of the introduction of a bottle into the rectum by a patient, with perforation of the bottle through the rectosigmoid into the general peritoneal cavity. The bottle was removed by laparotomy and the laceration of the colon sutured and a cecostomy performed. The postoperative course was complicated by a pelvic cellulitis which responded satisfactorily to aureomycin therapy.

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UNEXPLAINED GASTROINTESTINAL BLEEDING DUE TO A BENIGN TUMOR OF THE SMALL INTESTINE

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INTRODUCTION

MODERN practice demands accurate diagnostic evaluation of all patients prior to submitting them to surgery. Occasionally, the diagnostic studies fail to provide a clue as to the source of the disease and surgery becomes necessary to save the patient's life. Rarely, as in this case, diagnostic studies could not be performed because of the patient's extremely poor condition. We have recently seen a case of massive gastrointestinal bleeding that was undiagnosed before surgery, and which we believe to have been undiagnosable by any means at our disposal other than surgical intervention.

The lesion in this case consisted of a pedunculated fibroma of the ileum; the fibroma grew away from the lumen of the ileum. The mucosa of the ileum underlying this tumor was slightly dimpled, and there was an erosion of the mucosa at this point; this erosion was the source of the bleeding. There was no constriction of the lumen or any deformity which would have been visible by x-ray.

This is a rare lesion. Raiford's[1] excellent review indicates benign tumors comprise only 5 per cent of all gastrointestinal lesions. Other excellent reviews attest to the rarity of finding a small intestinal benign tumor.[2-4] Despite the rarity and difficulty of preoperative diagnosis when unexplained gastrointestinal bleeding occurs, a tumor of the small intestine should be considered in the differential diagnosis.

CASE REPORT

Mr. J. R., a 56-year-old white married merchant, was referred to one of us because of the passage of dark red and tarry stools of five days' duration. The patient stated that he had had some vague bloating sensations in the upper abdomen for 15 to 20 years. These usually appeared in about 1 hour after eating a very heavy meal and would not disappear before 4 to 5 hours. They were not accompanied by pain, nausea, vomiting, or change in the appearance of the stool. About 2 years prior to admission the patient had a brief febrile attack which was followed by jaundice of 2 weeks' duration; the patient's physician felt that this probably represented a bout of infectious hepatitis, and because of the spontaneous recovery no further studies were performed. Five days prior to admission, without any antecedent illness or associated symptom, the patient began passing tarry and dark red stools. His red blood cell count fell rapidly despite transfusions by his local physician. Because of failure to respond and because the site of the lesion was unknown, the patient was sent to St. Vincent's Infirmary for further diagnostic studies and treatment.

The family history disclosed that one sibling died of cancer, but otherwise it was not remarkable. Social habits and past history were noncontributory. A complete systemic review disclosed only labile hypertension.

Physical examination disclosed a rather pale, somewhat anxious, slightly bald white man who seemed acutely ill; he appeared somewhat obese and well developed. Temperature was 98° F., blood pressure 140/86, pulse 100, and respirations 22. The head, the mouth, the special senses, the lungs, and the heart were entirely negative. The abdomen was somewhat protuberant; it was soft throughout, and there was no muscle guarding or tenderness; good bowel sounds were audible. The liver and spleen were not palpable nor were any

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masses felt. The rectum and anus were not remarkable. Gentials and extremities were normal. No spider telangiectasis was found in the skin, and there was no visible jaundice.

Laboratory Studies on Admission.—Urinalysis done April 7, 1949, on a straw-colored voided specimen, showed pH 5.5 and specific gravity 1.020. The specimen was negative for albumin, acetone, sugar, red blood cells, and epithelial cells. An occasional white blood cell was present. The stool was strongly positive for occult blood.

Blood test data are given in Table I.

TABLE I

DATE	RED BLOOD CELL COUNT (MILLIONS)	WHITE BLOOD CELL COUNT	HEMOGLOBIN (GM.)	POLY-MORPHONU-CLEARS	LEUCO-CYTES	MONO-CYTES	EOSINO-PHILS
4/ 7/49	2.18	11,850	6.7 (40%)	79	20	1	
4/ 9/49	3.47	8,800	8 (65.8%)	78	19	1	2
4/10/49	3.3	12,500	11	69	29		2
4/19/49	4.67	9,500	15	55	42	1	2

Special Laboratory Studies.—Nonprotein nitrogen was 45 mg. per cent. Bleeding time was 3 minutes, clotting time 3 minutes. Thymol turbidity was 0.2 units, bromsulfalein (5 mg. per kilogram) 22 per cent at 30 minutes, and prothrombin time, 79 per cent.

X-Ray Studies.—It was felt that the patient was too ill to get x-ray studies of any sort.

Course.—A Levine tube was passed and no blood was obtained from the stomach. The laboratory studies indicated no clotting defect or prolongation of the bleeding time. The bromsulfalein test was equivocal; it definitely was abnormal, yet in the face of the bleeding and the negative thymol turbidity, it was felt that only limited trust could be placed in this test. Moreover, if the patient had cirrhosis and esophageal varices the Levine tube should have brought up some blood. The patient recognized the onset of each hemorrhage; he would feel weak and then pass a bloody stool. He had 5 such major bleeding episodes.

The continued bleeding made it seem advisable to perform surgery if the patient's life was to be saved.

Operation.—Through a right mid-rectus incision the abdomen was opened and explored (H. G. H.). In the mid-portion of the ileum a polypoid mass was found hanging free in the abdomen and attached by a narrow stalk to the ileum. Superior to this point the intestine contained little or no blood. Inferior to this point the intestine contained a large quantity of blood. The ileum was resected for a distance of 5 cm. above and below this point, and an end-to-end anastomosis of the bowel was done.

The patient made a rapid and uneventful recovery and had no further gastrointestinal bleeding.

Pathologic Report.—The gross specimen consisted of a segment of small intestine measuring approximately 12 cm. in length. Appended to the serosal surface was a pedunculated tumor mass measuring approximately 6 by 6 by 6 cm. in its largest diameter. The tumor had a pinkish-red color and a firm, somewhat elastic, consistency. The cut surface of the tumor had a somewhat tawny color and was not otherwise remarkable. The ileum was opened parallel to the longitudinal axis. At the point of attachment of the tumor there was a very small dimple in the mucosa which measured less than 3 by 1 mm. There was a very small erosion in the center of this dimple measuring at the most not over 2 mm. The ileum was not otherwise remarkable.

Microscopically, a section showed fibrous tissue and fibromuscular bands. There was no rosette formation and no palisading could be seen. The spindle cells were slightly thickened in some areas. Impression was fibroma of the ileum.

DISCUSSION

This case differed from a recent case of unexplained bleeding from the gastrointestinal tract reported by Edwards.[5] In the latter the tumor was visible

by x-ray; the tumor reported by us would have been invisible despite the careful x-ray techniques that are reported by various authors.[3, 4, 6, 7] Perhaps it would have been possible in this instance to have passed a Miller-Abbott tube and tried serial aspirations for blood, but the patient's condition made it seem unwise.

Rankin and Grimes[8] had an experience similar to ours in that they were forced to operate on a small bowel tumor in the face of negative laboratory studies. It ought to be emphasized again that no patient bleeding from the gastrointestinal tract should be explored without a thorough case work-up. However, if the case work-up discloses no valuable clues as to the pathology and if the patient's condition deteriorates, surgery should be performed despite the negative work-up, and the small intestine should be carefully explored to rule out a tumor.

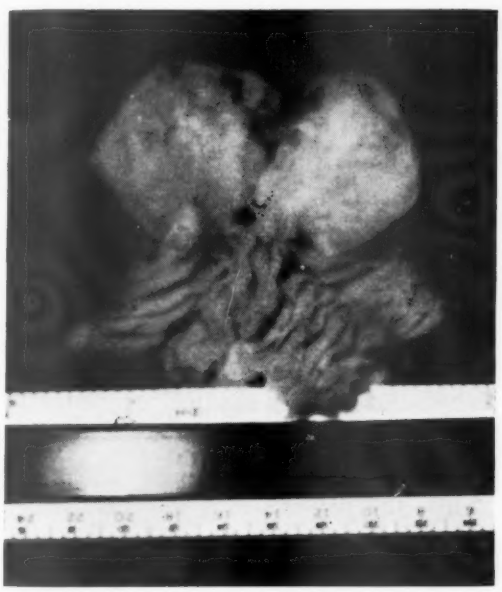

Fig. 1.—Gross specimen of the fibroma cut transversely.

SUMMARY

This case is reported because of the rarity of benign small bowel tumors which grow away from the intestinal lumen. The tumor caused massive gastrointestinal bleeding which could not have been diagnosed prior to surgery.

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Editorial

Mobilization and the Training of Doctors

We are in the midst of a vast mobilization of manpower for the armed forces. Of necessity thousands of physicians must be recruited. As far as one can tell, there exists no orderly plan to make certain that we continue to train the scientists upon whom the future so heavily depends, or, to speak more specifically of that branch of science with which we are particularly concerned, to train the doctors who will become the teachers, the investigators, the leading practitioners of tomorrow. The tragedy of this situation cannot be overemphasized. Continuance of the present policy can only lead to future scientific and medical bankruptcy.

The future is in the hands of our youth. Unless we prepare a reasonable number of them for the leadership which they must assume, we cannot expect them to cope with the difficult problems they will inherit or to carry on the professional advance which will be so urgently needed. We cannot give them a curtailed or half-hearted training. We must give to some of them the very best of which we are capable. Already within a decade we have been engaged in one long war during which the better type of residency training virtually ceased to function and the training of men in clinical and laboratory investigation was practically at a standstill. Years followed when large numbers of ambitious doctors besieged the various medical centers with heart-rending supplications for such opportunities. The result was a harassing situation—overcrowding among the house staffs and in the research laboratories—men marking time, so to speak, until the passage of years and the elimination of some of their competitors would create for them some measure of real opportunity and responsibility. A repetition of another such decade will be disastrous. Something must be done to permit the continued training of a reasonable number of young men—thoroughly, completely, enthusiastically.

Preservation of the residency training and research programs has as its principal objective this continued output of men with promise of leadership and top-flight performance. There are, however, other reasons for their continuance. In the first place, if we destroy the system of residency training there will have to be put into effect some other means for accomplishing that part of hospital care now entrusted to the resident staff. And with the dawn of a new day the entire program will have to be reborn, in many institutions with the same heartaches and struggles which characterized its original introduction. The research laboratories, needed as sorely in time of war or national stress as in time of peace, but rendered more or less useless by depletion of personnel, will tend to be gobbled up by other activities of our space-starved hospitals and medical schools. And some day they too will have to be reconstructed piece by piece. Remove the postgraduate student and the facility for training him will crumble.

Another aspect of the problem might be emphasized, namely, the important role played by the young doctor-in-training in the proper care of patients and in the teaching of medical students and interns on the wards and in the clinics. It would, however, appear unwise to lay stress upon this aspect of the matter. Institutions of all sorts will suffer from lack of personnel. All will have to devise ways and means of accomplishing their objectives with reduced manpower by dint of better organization and longer and more intensified work. The same will be our problem in the hospitals and in the medical schools. The proposition that the training of physicians and surgeons, teachers and investigators should proceed in spite of war, or the threat of war, must stand upon its essentiality in providing the future with the men it needs and in preserving the mechanism by which such men are trained.

Is such a program possible? Let us examine the case. First, everyone will agree with the necessity for the rapid expansion of our armed forces. We can count ourselves lucky indeed if a suitable fighting force can be brought into being rapidly enough to compel peace or to meet further aggression. Secondly, a large military establishment requires a large medical department. We may argue among ourselves the proper ratio of medical officers and military personnel. We may recall with distaste the long periods of professional inactivity which have occurred from time to time in every war. We may postulate ways and means of utilizing more effectively the total medical component of the armed forces, and, if such ideas seem promising, we may try to bring them to the attention of military authorities who might lend a willing ear. The fact remains that we cannot compromise; our Army, Navy and Air Force deserve and are going to have the best of medical care and large numbers of doctors are going to be required. It is a fact that war, and to a lesser extent preparation in the hope of preventing war, are necessarily wasteful of medical manpower. No one can eliminate the peaks and the less demanding periods of medical activity resulting from the unpredictable and variable occurrence of illness and, more particularly, from the waves of casualties which follow combat activity. No one can eliminate the time consumed in the training of troops or in the transportation of armies to distant battlegrounds. We may legitimately demand of the military the commissioning of the minimal number of doctors required. None the less the number is staggeringly large.

Can we meet this demand and yet continue to take care of the civilian population and at the same time train men for the future? I believe it is possible. To be sure, deferment of military service until completion of training will have to be granted a considerable number of those men in categories one and two of the present draft code and of those who will be graduating in medicine in the years ahead. From all available estimates of the military needs on the one hand and the number physically and mentally qualified on the other, such action would likely necessitate the recruiting of many from other groups. I can see no inherent objection to this policy. Perhaps too much emphasis is being placed upon the obligation for immediate military service of those in the first two categories. It is clear that these individuals do owe their nation a particular debt of gratitude, not only for having been given the opportunity to

complete their medical education, but also for having been spared the hardships and dangers to which millions of their comrades were subjected. The obligation or privilege of serving one's country in time of need, however, is universal and is not limited solely to the young nor to any special group. And who among us does not owe her a similar indebtedness? Let us, for example, consider the older physicians who have had no military service. During the years of World War II they worked untiringly, to be sure, and to the everlasting credit of our profession carried on their civilian duties with reduced numbers and under adverse circumstances. Yet by and large their rewards were ample. They were able to continue in their chosen field of work. They were able to advance their status as practitioners, teachers, investigators. By military pay standards they were well recompensed. Most important of all, they were spared the disruption of their professional and home lives and the difficulties and dangers to which so many others were subjected. Or let us consider those who have had military service. In spite of any sacrifice which this service may have necessitated, in spite of any hardships, risks or disappointments experienced, it is nevertheless true that most of us survived the experience and returned to civilian life hale and hearty. And all of us returned to a nation in which fundamental freedoms and opportunities were preserved. It would seem that the fairest rule of all would be the application of the simple principle that the last to be called into service should be those who have served before and served the longest, excepting, of course, those who by their own volition have chosen to retain commissions. If, in order to permit the continuation of the proper training of doctors, it is necessary to commission men from the older groups without prior service, or to recall to service numbers of us who have served before, the nation will not suffer in the long run. It can as easily afford to risk its mature manhood as its promising youth.

It is recognized that the actual management of a policy of continued training of doctors presents many practical difficulties and I do not presume to know the best method. A just plan should not, however, be difficult to conceive and put into operation. The following would appear to be workable, though it is not presented as the final solution of the problem. Let us suppose, for example, that we should decide to continue to train one-half the number currently being trained. Perhaps this number is too large but it will at least serve as a point for discussion. The various specialty examining boards, or some similar agencies, might be asked to select as training centers three-fourths of the hospitals now approved, those best equipped to carry on such training. Each of these hospitals might be permitted to continue to train two-thirds of those currently in training. Appointments would be made by the approved services on a competitive basis, just as they are at present. Deferment for those selected would be more or less automatic. At the completion of a first-rate training program these individuals could then be brought into the armed forces. They would serve them well and they would guarantee to our country the leadership the future demands. There could be no better way of showing our confidence in our future than the provision for such able leaders.

—H. B. Shumacker, Jr., M.D.